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ROENTGENOLOGIC DIAGNOSIS

Changes Resulting From Chemotherapy

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Roentgenologic diagnosis is based on the interpretation of variations in gross pathologic conditions as they are recorded on the roentgenogram or depicted on the fluoroscopic screen. There are certain criteria on which a fair degree of reliance may be placed in making diagnoses of infectious processes. Not only may these changes due to infection be recognized, but frequently sound judgments may be made in regard to the stage of the infectious process, and by successive examinations a fairly accurate idea may be gained of the progress of the disease and its probable outcome.

In the interpretation of roentgenologic observations in infections consideration must be given to the possible modifying effects of any therapeutic measures which have been used. Hitherto there was usually little difficulty in evaluation of the changes in the roentgenologic-pathologic picture resulting from therapy. This is no longer true since the advent of the sulfonamide compounds, penicillin and allied products. These drugs have not only profoundly modified the clinical aspects of infectious diseases but produced significant changes in the pathologic-anatomic manifestations, with a resultant change in their roentgenologic-pathologic appearance.

Never before has the body been called on to handle a situation in which there has been complete or partial arrest of an infectious process by the artificial killing or attenuation of the infecting organisms in situ. When all of the organisms have been killed, the resultant tissue responses and their roentgenologic manifestations present new phenomena. This is also true to a lesser extent when the organisms are abruptly attenuated and an active acute infection transformed into a low grade chronic state. These changes must be kept in mind and given careful consideration in the interpretation of roentgenologic observations. This is especially important in view of the common and widespread use of these new drugs in treatment against infections.

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Read before the Section on Radiology at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 4, 1946.

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The following cases, with brief histories and accompanying roentgenograms, are presented for illustration and emphasis of the necessity for giving special attention to the diagnostic problems which may be encountered:

REPORT OF CASES

CASE 1.—A white boy aged 4 was admitted to the hospital Oct. 15, 1944 during an attack of pustular chickenpox, the eruption of which appeared October 10. His temperature was 104 F. from October 12 to 15. On October 14 his right wrist had become swollen, red and extremely tender. He was placed on a regimen of parenterally administered penicillin on admission, receiving a total of 1,510,000 units over a period of eleven days. The acute tenderness and swelling began to subside on the second day, and within a week little tenderness remained. After the second week the only clinical residuum consisted of slight limitation of motion of the wrist, and this also had disappeared at the end of one month. The patient remained asymptomatic thereafter. A roentgenogram taken two days following the onset of symptoms did not show abnormality of the bones. There was edema of the soft tissue about the entire circumference of the distal ends of the radius and ulna, an observation which was considered consistent with early osteomyelitis. A film taken two days later showed a small area of osseous destruction with a break in the cortex, forming a cleft in the extreme distal ventral aspect of the radius. A definite diagnosis of osteomyelitis was made at this time. Figure 1 demonstrates the healing process of osteomyelitis. Eleven months following the onset only a scar remained at the site of the original disease. The bone which had grown beyond this scar appeared normal.

This case illustrates the manner in which the body handles osteomyelitis in which the organisms have been killed by adequate penicillin dosage during the early acute stage of the disease. The series of films presents a fairly complete and understandable picture. If, however, a single roentgenologic examination had been made at one of the stages in which subperiosteal bone was present, interpretation would have been rather difficult as based on the manifestations of osseous infection before the advent of chemotherapy.

CASE 2.—A Negro woman aged 24 was well until about Dec. 28, 1944, when "tonsil infection" developed, as she was told by her physician. About two weeks following this infection a sudden severe, sharp, continuous pain developed in her right thigh just above the knee. This later extended up the thigh almost to the hip. About three weeks later she was still complaining of pain and tenderness. At that time her temperature was 99.6 F. She had a leukocytosis of 18,800 with 70 per cent neutrophils and a sedimentation rate of 27 mm. by the Wintrobe method. Roentgenologic examination of the right femur at that time showed no abnormality whatever. The patient was given 18 Gm. of sulfadiazine over a period of forty-eight hours. She did not report again until March 21, 1945. Roentgenologic examination of the right femur at that

time (fig. 6*A* and *B*) showed extensive motheaten osseous destruction involving the entire shaft of the right femur with elevation of the periosteum and a deposit of subperiosteal new bone. The white blood cell count was 10,000 with 73 per cent neutrophils and a sedimentation rate of 30 mm. by the Wintrobe method. The patient refused to submit to a surgical procedure. She was admitted to the hospital and 1,600,000 units of penicillin were given parenterally over a period of eight days. The pain and tenderness slowly disappeared, and at the end of two months she was practically symptom free. She was last seen Jan. 18, 1946, at which time she complained of occasional pain in the right thigh but was otherwise well. A roentgenogram taken at that time (fig. 6*C*) showed apparently complete healing of the osteomyelitis with decided thickening of the cortex of the femur.

This case illustrates a more advanced stage of osteomyelitis, in which treatment was started later. The final appearance is more that of osteitis deformans than that of any other entity. The irregular osseous destruction and sequestration due to chronic osteomyelitis which was seen in earlier roentgenograms is not present.

Case 3.—A white man aged 28 was first seen elsewhere in February 1944, at which time a diagnosis of nasal accessory sinusitis was made and he was placed on a regimen of sulfanilamide therapy for twelve days. The sinusitis subsided. On March 28, 1944 he was again seen with symptoms of dull aching pain in the anterior portion of the left thigh and with radiation of the pain to the knee. The symptoms subsided with rest, but in August 1944 the pain returned and a small mass was noted in the upper posterolateral portion of the left

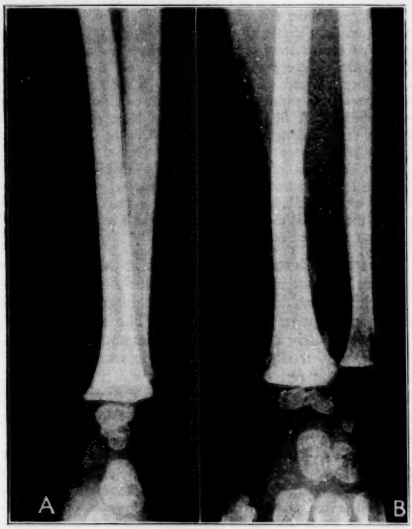

Fig. 1 (case 1) *A*.—There is a small deposit of new bone beneath the elevated periosteum. *B*. One and one-half months following onset the subperiosteal new bone has assumed a nodular form. A diagnosis of osteogenic sarcoma might be made if this were the only examination.

thigh. A roentgenogram made at this time was the basis for a diagnosis of osteogenic sarcoma (fig. 2). There was an increase in the density of the mid shaft of the femur with almost complete obliteration of the medullary canal and proliferation of new bone about the periphery of the femur with spicules radiating into a soft tissue mass. The appearance simulated that of osteogenic sarcoma. There was, however, a sharply defined 8 by 13 mm. oval area of diminished density in the shaft at the lower margin of the lesion which did not have the appearance seen in cancer and represented a cortical abscess. A surgical operation was performed Sept. 12, 1944 and disclosed a soft mass composed of granulation tissue located adjacent to the posterolateral aspect of the mid femur, with a sinus tract measuring ½ inch (1.27 cm.) in diameter extending into

Fig. 2 (case 3).—Lateral view of the femur.

Fig. 3 (case 5).—Oblique view of the distal part of the ankle and leg showing slightly irregular subperiosteal new bone with a knoblike projection of new bone toward the tibia. This knob is higher in position than an exostosis, which it simulates. Similar bony projections have been seen in 2 other cases similarly treated. The general appearance is much like that of syphilitic periostitis and angioendothelioma.

the bone. Free pus was present in the sinus tract. The patient was placed on intensive penicillin therapy, and subsequent roentgenologic examination revealed that the new bone had begun to assume normal architecture.

This illustrates a circumstance which will probably become increasingly frequent with the more widespread use of chemotherapy. The amount of sulfanilamide administered was sufficient to control the sinusitis, but larger doses and more prolonged administration are required to control infection of bone. It may be assumed that the osseous infection in this instance occurred at the time of the sinusitis, since there was no history of infection elsewhere. Symptoms of the infection of the bone did not occur, however, until after a lapse of over a month, and even then the process was an extremely low grade one. The roentgenologic appearance is extremely bizarre, and the diagnosis of osteogenic sarcoma is understandable. It seems reasonable to assume that the prolonged course and unusual roentgenologic picture is the result of definite attenuation of the infecting organism by inadequate chemotherapy.

Case 4.—A white man aged 24 was first seen elsewhere in October 1945 and was treated with sulfanilamide for an upper respiratory infection, which subsided. About one month later he noticed pain and tenderness in the calf of the right

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leg; the symptoms were aggravated by walking. They increased in severity, and in December 1945 he was admitted to a hospital. A roentgenogram made at that time revealed essentially the same conditions as those seen on Jan. 14, 1946, when there was a sharply defined area of osseous destruction involving the lateral aspect of the cortex of the mid portion of the fibula for a distance of 4 cm. The lesion was expansile in character and had fairly smooth margins. In the center of the lesion there was a 1 by 8 mm. vertical spicule, which had the appearance of a sequestrum. The lesion as a whole, however, was not characteristic of any particular entity. In appearance it simulated fibrous displasia more than any other disease. The original diagnosis was possible bone cyst and the second, cortical bone abscess modified by chemotherapy.

The lesion was resected, and its histologic appearance was that of healing osteomyelitis.

CASE 5.—A white woman aged 44 first noticed pain and swelling of her right ankle in July 1945. The history did not disclose any preceding illness, infection or injury. She was seen elsewhere and treated with penicillin by mouth, sulfonamide compounds and diathermy. The exact dosages are not known, but from the patient's history the chemotherapy was neither intensive nor prolonged.

The symptoms abated, but after a few weeks they became progressively more severe. She reported to another physician, who requested the roentgenogram taken April 18, 1946 (fig. 3). A diagnosis of osteoperiostitis modified by chemotherapy was made, and she was admitted to the hospital. The Wassermann test was negative. The sedimentation rate was 16 mm. by the Cutler method. She received 1,475,000 units of penicillin parenterally over a period of eight days. She gradually improved and became practically asymptomatic two months after treatment.

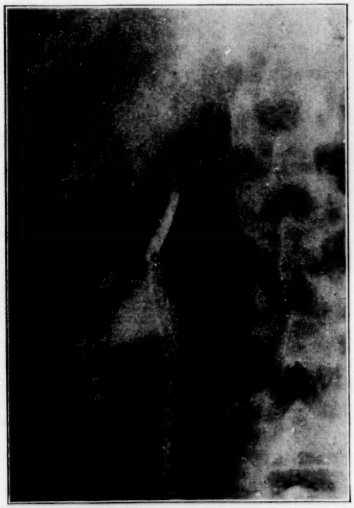

Fig. 4 (case 6).—Pyelogram taken in Germany on Aug. 11, 1944 showing enlargement of the upper pole of the right kidney and a slight pressure deformity of the upper calyx.

This case again illustrates the effect of inadequate treatment on infection; in this instance the method of treatment was the oral administration of penicillin, which requires such huge doses in order to be effective that the cost of the oral method is still prohibitive in most patients. The roentgenologic picture strongly resembles syphilitic periostitis except for the knob of bone projecting toward the tibia. This "knob" has been seen in 2 other cases similarly treated. Except for the knob the possibility of angioendothelioma should be considered.

Confusion has long existed in the differential diagnosis roentgenologically between tumor and syphilis in both bone and soft tissue. The same confusion now extends to any infection which has been altered by chemotherapy or penicillin.

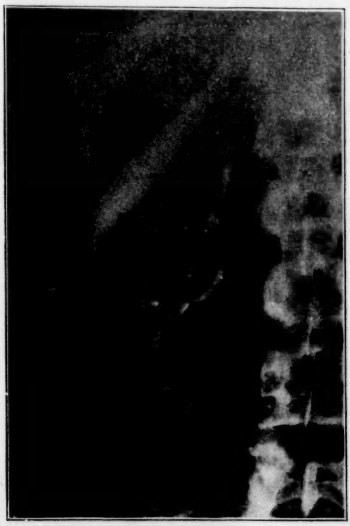

Fig. 5 (case 6).—Pyelogram taken Sept. 15, 1945 showing extensive pressure deformity of the calices of the right kidney from a mass either in or adjacent to its upper lateral portion. This film also shows a narrow line of diminished density along the adjacent margin of the liver which has the appearance of gas. The right kidney is fixed in position, and the right side of the diaphragm limited to about one-half the excursion of the left. The appearance is that of a perinephritic abscess, part of which is probably within the renal capsule, with gas in the soft tissues peripheral to the kidney.

CASE 6.—A white man aged 23 [1] was admitted Sept. 13, 1945 complaining of general malaise and a slight elevation of temperature to 99 F. in the evenings. Physical examination revealed a hard, fixed mass in the right upper quadrant of the abdomen. The patient had complained of abdominal pain on the right side intermittently for two years. Prior to this he had an attack of carbuncles which cleared spontaneously. At the time of, or shortly after, the carbuncles he contracted gonorrhea for which he received 200,000 units of penicillin. During part of the prolonged chronic illness the patient was a prisoner in Germany, at which time the first roentgenologic examination was carried out (fig. 4). A diagnosis was not made at this time. In the interval he lost 40 pounds (18 Kg.). The first diagnosis on subsequent examinations after the patient's return to the United States was renal tumor. The final diagnosis at the last examination (fig. 5) was perinephritic abscess, based on the presence of gas within the mass. A surgical operation was performed Sept. 18, 1945. A tremendously thick, hard mass of scar tissue was encountered in the region of the upper pole of the right kidney. When an incision was made through this scar tissue a large perinephritic abscess was opened and approximately 1,000 cc. of light green pus was evacuated.

1. Lewis, L. G.: Diagnosis of Perinephric Abscess, S. Clin. North America **26**: 337 (April) 1946.

This case illustrates the effect of inadequate penicillin therapy on an abscess of the soft tissue, the presence of which was unsuspected. Perirenal abscesses may be extremely chronic, but certainly two years is an unusually long duration. The abscess evidently began as a cortical abscess of the kidney, and its extremely slow growth resulted in a large, hard inflammatory renal and perirenal mass with decided distortion and compression of the renal calices simulating tumor or cyst.

SUMMARY AND CONCLUSIONS

1. Roentgenologic diagnosis is based on gross pathologic variations from normal in tissues which are visible by roentgen ray.

2. Through experience, the changes produced by infection had become known and their various stages catalogued to such an extent that not only diagnosis but prognosis was possible.

Fig. 6 (case 2).—*A*, there is an area of moth-eaten osseous destruction involving a 6 cm. length of the distal shaft of the femur, with new bone beneath the elevated periosteum extending upward from this area. *B*, view of the remainder of the femur taken on the same date as *A*. The entire shaft of the femur is involved by irregular destruction largely limited to the outer aspect of the cortex. The whole is surrounded by subperiosteal new bone which is slightly laminated in character. *C*, seven and one-half months later there is no roentgenologic evidence of active infection. The cortex is extremely thick, and its appearance simulates that of osteitis deformans.

3. The sulfonamide compounds and penicillin have altered not only the clinical but the pathologic anatomic aspects of infection.

4. The most significant and previously unknown condition which results from inadequate treatment with these agents is that infection, the activity of which has been arrested completely or partially by artificially killing or attenuating the infecting organisms, leaves the tissues of the body to dispose of the resulting debris.

5. Body tissues have never been called on to handle such a situation. This altered reaction to injury of the body tissue by infection often simulates neoplasm and, as has been demonstrated, may be easily confused with cancer, syphilis and other conditions.

6. Chemotherapy is so commonly used that its effect must be kept in mind and investigated whenever an unusual roentgenologic or clinical observation is made.

ABSTRACT OF DISCUSSION

DR. L. H. GARLAND, San Francisco: The antibiotics can sterilize a bone or soft tissue infectious process in midflight and leave the gross pattern of disease to confuse the clinical radiologist. Drs. Christie and Wyatt remind us once again that bacterial diagnosis is seldom possible by individual roentgenologic examination and that the newer drugs make even the diagnosis of active inflammation difficult. Their observations emphasize the fact that we are dealing in shadows of gross processes and that we tend to "overread" those shadows. Intelligent roentgenologic examination of diseased tissue (notably of bones and joints) requires that the interpreter have some information concerning the principal symptoms or clinical signs which happen to be present plus some facts on the medicaments administered to date. Without these facts the most expert radiologist may be led to erroneous conclusions. I have seen a sequence of events similar to those noted in case 1 in a few cases of mild infection of the long bone treated with roentgen radiation. They represent fairly prompt healing (and might have eventuated even without the small doses of irradiation given). The authors use the adjective "apparent" before the word "healing" in describing the final roentgenologic appearance in case 2. This is important. It is known that infection may be suppressed but not destroyed in some patients treated with antibiotics. The gross appearance becomes encouraging, only to break down at a later date. The florid or productive type of osteoperiositic lesions seen in case 3 may simulate osteogenic sarcoma or vice versa. I have seen cases of bone tumor in which needle or incisional biopsy gave no definite evidence of tumor. I wonder if the authors would not diagnose case 6 as a carbuncle of the kidney, later followed by a perinephric inflammatory mass. The interpretation of the radiolucent zone as gas is open to question. The authors have probably seen some cases of mastoiditis in which sulfonamide or penicillin medication profoundly modified the roentgenologic appearance. To me this is one of the most perplexing phases of this question. We are indebted to Drs. Christie and Wyatt for reminding us that criteria for the diagnosis of disease from roentgen shadows are, like so many other clinical phenomena, highly evolutionary and changeable but nonetheless simple and clearcut provided the basic factors of roentgenologic interpretation are constantly borne in mind.

DR. LOWELL S. GOIN, Los Angeles: I dissent from the statement that syphilis is the only lesion that can be confused with bone tumor. In my experience angioendothelioma is always confused with infectious disease, and osteogenic sarcoma is frequently the same. When the body is invaded by bacterial infection, it summons all its natural resources and alterations in the local and general behavior of the body begin at once. All the usual pathologic changes that accompany infection are found. The bacterial invasion overwhelms the patient, nature overwhelms the infection or the balance is such that neither is quite successful, and we encounter such states as long-standing chronic osteomyelitis. If large amounts of antibiotics are given a patient and the bacterial infection is suddenly overwhelmed, we find we do not have the complete alteration in the roentgenologic

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appearance of the repair processes that we would expect, and this is what leads to confusion. There are only two changes in bone which can be recognized by roentgenologic examination—bone destruction and bone production. It is a recognition of these two changes and the summation of their variance on which the diagnosis of all bone disease rests. If some alteration occurs that changes the character of the destruction or production, prevents the production to the point where it would have been expected or limits the amount of destruction that occurs, then we have the confusing pictures that the authors have drawn to our attention.

DR. GEORGE M. WYATT, Washington, D. C.: I want to emphasize the main point we are trying to get across, namely to be on the lookout for these inadequately treated patients. You will notice that these patients were cured after they received adequate treatment, and what we must think about is the welfare of the patient. In regard to the kidney case, the diagnosis was renal cortical abscess followed by perirenal abscess. In regard to syphilis there has been for a long time confusion between the changes seen in syphilis, angioendothelioma and other bone tumors, whereas previously we only occasionally ran across a low grade infection which simulated both syphilis and tumor. Now with the modification of infections by chemotherapy we are going to see this similarity with increasing frequency.

ALLERGY TO VIRUS AND RICKETTSIAL VACCINES

I. Allergy to Influenza A and B Vaccine in Children

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One of the sound principles of allergy is that whenever the host is the recipient of a foreign substance, repeated invasions may result in a hypersensitivity to that substance. It follows, therefore, that the introduction of virus and rickettsial vaccines prepared from cultures grown in chick embryonic tissues must carry in its wake the phenomena of allergic reactivity. An intriguing aspect of the allergy induced by these vaccines is that the allergenic components responsible for these reactions are related to egg-chicken proteins, substances common to the diet.

Approximately 10 per cent of allergic persons are sensitive to egg and its related proteins. If the allergic population comprises 10 per cent of the total population, then 1 per cent of the general population is sensitive to egg in varying degrees. This sensitivity is spontaneously acquired through ingestion. With the advent of these newer vaccines, millions of persons have already had egg proteins introduced into them parenterally. It is possible that through this novel method of introducing a food protein, some persons may later become hypersensitive to egg-containing foods. Stull [1] has already demonstrated such an instance.[2]

The following general types of vaccines are considered in this paper: (1) yellow fever vaccine, grown on chick embryo tissues; (2) equine encephalomyelitis vaccine, grown on chick embryo; (3) typhus vaccine, grown on chick yolk sacs; (4) Rocky Mountain spotted fever vaccine, grown on chick yolk sacs (the last mentioned has also been made from combined yolk sac and chorioallantoic membranes—a so-called membrane vaccine), and (5) influenza A and B, grown in chick embryo chorioallantoic fluid.

ANAPHYLACTOGENIC PROPERTIES OF EGG-CHICK EMBRYO VACCINES

Well defined local and systemic reactions, terminating fatally in some instances, have been reported by Schoening [3] in horses after reinjection of equine encephalomyelitis vaccine. Similar observations were made by Wolfe and Trum [4] and by Graham.[5] Wolfe and Trum also observed apparently typical desensitization following recovery from anaphylactic shock. Because of allergic reactions, Schoening and his co-workers [6] suggested that vaccination be made by the intradermal route with small volumes of the vaccine. Satisfactory results have been reported from the use of this procedure.

Van der Scheer, Wyckoff and Bohnel [7] showed that guinea pigs can be sensitized with equine encephalomyelitis vaccine and fatally shocked on receiving a second inoculation. However, when Rocky Mountain spotted fever vaccine prepared from combined yolk and chorioallantoic membranes according to the method of Cox [8] was used for sensitization, they were unable to produce anaphylactic shock in the animals.

So far as ability to produce anaphylaxis in guinea pigs can be taken as a measure of capacity to sensitize man, it would appear that a vaccine grown on membrane can be administered with less danger of reaction than can a vaccine grown on entire embryo. Vaccines grown on membrane, such as typhus vaccine, contain less tissue than equine encephalomyelitis vaccine made from chick embryo, for even large amounts of the former did not produce a reaction, whereas a twenty-fold dilution of the latter was still an effective agent.

These experiments of van der Scheer and his associates indicate that vaccines grown on membrane (typhus and other rickettsia) are preferable to those grown on entire embryonic tissue, so far as sensitization is concerned. This fully corroborates the studies of Cox,[9] who also failed to induce sensitivity with Rocky Mountain spotted fever and typhus vaccines grown on membrane. Coulson and Stevens [10] showed that suspensions of washed rickettsial bodies contain egg antigens, but in a much lower concentration than that present in the egg yolk sac. Their studies indicated that such suspensions contain egg antigens in quantities which are near the minimum sensitizing dose.

Berge and Hargett,[11] employing yellow fever vaccine and crude extracts from normal chick embryos, found that in guinea pigs chick embryo extract from 10 day or younger embryos is weakly anaphylactogenic, while that from 14 day embryos is highly so. They suggested the use of younger embryos in preparing vaccine in order to reduce the anaphylactogenicity of these biologics.

From the Department of Pediatrics, New York University College of Medicine.

1. Stull, C. A.: III. A Study to Determine Whether Chick Egg Yolk Sac Vaccines Contained Sufficient Egg Proteins to Cause Severe Systemic Reactions if Given to Egg Sensitive Individuals, J. Immunol. **53:** 343, 1946.

2. The studies of Plotz,[18] Coulson and Stevens [10] and Stull [1] were presented as a joint investigation under the general title of "Allergenic and Anaphylactogenic Properties of Vaccines Prepared from Embryonic Tissues of Developing Chicks," at the meeting of the American Association of Immunologists, held in Atlantic City, N. J., March 1946.

3. Schoening, H. W.: Reactions Following Administration of Equine Encephalomyelitis Vaccine, J. Am. Vet. M. A. **97:** 39, 1940.

4. Wolfe, W. R., and Trum, B. F.: Anaphylactic Reactions Following the Use of Chick Embryo Equine Encephalomyelitis Vaccine, Vet. Bull. U. S. Army **34:** 226, 1940.

5. Graham, R.: Reactions in Horses Following Inoculation of Chick Embryo Vaccine, J. Am. Vet. M. A. **97:** 38, 1940.

6. Schoening, H. W.; Shahan, M. S.; Osteen, O. L., and Giltner, L. T.: Studies on the Intradermal Method of Vaccination Against Equine Encephalomyelitis, Vet. Med. **35:** 377, 1940.

7. van der Scheer, J.; Wyckoff, R. W. G., and Bohnel, E.: Antigenicity of Chick Embryo, J. Immunol. **41:** 349, 1941.

8. Cox, H. R.: Rocky Mountain Spotted Fever: Protective Value for Guinea Pigs of Vaccine Prepared from Rickettsiae Cultivated in Embryonic Chick Tissues, Pub. Health Rep. **54:** 1070, 1939.

9. Cox, H. R.: Cultivation of Rickettsiae of the Rocky Mountain Spotted Fever, Typhus, and Q Fever Groups in the Embryonic Tissues of Developing Chicks: Theobald Smith Award Lecture, Science **94:** 399, 1941.

10. Coulson, E. J., and Stevens, H.: II. Anaphylactogenic Properties of Typhus Fever and Equine Encephalomyelitis Vaccine, J. Immunol. **53:** 321, 1946.

11. Berge, T. O., and Hargett, M. V.: Anaphylaxis in Guinea Pigs Following Sensitization with Chick Embryo Yellow Fever Vaccine and Normal Chick Embryos, Pub. Health Rep. **57:** 652, 1942.

Further pertinent data on the anaphylactogenic properties of chick-egg vaccines is offered by Coulson and Stevens.[10] In general, the principal antigenic constituents in egg yolk sac vaccines, e. g., typhus vaccine and chick embryo vaccines, e. g., equine encephalomyelitis vaccine, are identifiable with antigens of fresh egg. Comparison of the anaphylactogenic activity of equine encephalomyelitis and typhus vaccines shows that, on the basis of protein nitrogen content, they are about equal in sensitizing capacity. On the other hand, the shocking capacity of equine encephalomyelitis vaccine is appreciably less than that of typhus vaccine. Coulson and Stevens attribute this to the heavier aggregation of the former vaccine's components, which serves to reduce the rapidity of absorption.

The sensitizing capacity of these two types of vaccines on a protein nitrogen basis, was found to be about one half that of egg white, and their antigenicity was related principally to the fresh egg white. These investigators found evidence that both typhus and equine encephalomyelitis vaccines contain antigens with specificity differing from that of egg white; but there was a lack of evidence that either vaccine contained antigen with specificity differing from that of combined egg white and egg yolk. Therefore, alteration of specificity of fresh egg proteins accompanying the organization of the protein into embryonic tissue during incubation could not be demonstrated.

These authors suggest that the results of their studies signify a possible hazard to potentially allergic persons and a definite hazard to those who are highly hypersensitive to egg proteins.

From the foregoing it would seem that chick embryo and embryonic fluids are highly antigenic and that vaccines grown on membrane and young embryo have a reduced anaphylactogenicity. Dr. Herald R. Cox[12] stated to one of us that if experience with reactions required it more of the antigenic material could be extracted.

HYPERSENSITIVITY REACTIONS TO VIRUS AND RICKETTSIAL VACCINES IN THE HUMAN SUBJECT

Eaton and Meiklejohn[13] in a series of 1,791 persons who received influenza vaccine noted but 3 cases of allergic reactions. In 1 patient a severe attack of asthma occurred within three hours after inoculation. A prior history of allergy was lacking. Urticaria developed in the second patient, and in the third, a probable urticaria.

Sulzberger and Asher[14] have reported 3 cases in which there is evidence for the assumption that yellow fever vaccine induced reactions: In 2 patients it resembled mild serum sickness, with urticarial and erythema multiforme eruptions occurring six and seven days, respectively, after injection; in the third there was a similar but accelerated reaction occurring in thirty-six hours. The cutaneous manifestations were accompanied by general malaise, pains in the joints, headache, fever, pruritus, nausea and vomiting. These observations indicate that this vaccine may potentiate hypersensitivity.

Swartz[15] has recorded a case of a severe constitutional reaction to a single immunizing injection of a mixed yellow fever and cholera vaccine occurring in a person aged 27. Less than five minutes after the injection the following symptoms ensued: blurred vision, labored breathing, nausea, vomiting, diarrhea, generalized urticaria and edema with increasing dyspnea, followed by unconsciousness. Symptomatic therapy with ephedrine and epinephrine resulted in a gradual abatement of symptoms, which finally subsided after six days. Two days later dyspnea and urticaria of a milder degree recurred, lasting for a period of two weeks. The patient's history disclosed that at 4 years of age he was fed large quantities of egg and egg white during an illness. From that time on, he was unable to eat eggs. He not only had an aversion to them, but the ingestion of the smallest amount of egg-containing food precipitated severe asthmatic paroxysms. He also was hypersensitive to other foods as well as to feathers.

Positive reactions to skin tests with allergenic preparations included a persistent and pronounced sensitivity to egg and chicken. Clinical tests performed on the patient with egg and chicken meat reproduced the symptoms previously described. His serum passively transferred sensitivity to the skin of normal recipients. Egg transferred 4 plus; chicken meat, 2 plus and yellow fever vaccine, 2 plus.

Since a virus is not known to be reaginogenic to produce cutaneous reactions of the immediate variety, Swartz has deduced that it was the culture medium fraction of the yellow fever vaccine that called forth the reaction. The fact that the skin test with cholera vaccine was negative contributes further to the conclusion that the allergic reaction must be related solely to the culture medium of the yellow fever vaccine.

Swartz expressed the opinion that so far as the egg white at all times caused stronger reactions than the chicken meat, this fact militates against the assumption of Berge and Hargett (given previously) that the age of the chick embryo has a direct bearing on the power to produce anaphylactic sensitization. If the assumption were correct, Swartz reasoned, the reactions would be related more closely to the chicken meat than to egg white.

This case vividly illuminates the importance of determining whether the recipient of this type of vaccine is hypersensitive to egg before proceeding with an injection.

Roth[16] has reported 9 cases of allergic reactions to typhus vaccine. Only 4 of the allergic reactors gave a history of allergy to egg, demonstrating that history alone is not a reliable criterion.

A typical case that Roth reported in a soldier aged 19 is here recounted. Immediately after the first injection of typhus vaccine the patient had extreme dyspnea, cough, weakness and substernal pressure. He had a temperature of 97.4 F., a pulse rate of 128 and a weak respiratory rate of 24. His skin was cyanotic and covered with an urticarial eruption; his face was edematous; his lungs were filled with asthmatic rales. The patient recovered in four days. Three days later, he was given 0.1 cc. of typhus vaccine, and a severe asthmatic attack followed immediately; but he did not have shock or cyanosis as before. He presented asthmatic rales, a temperature of 98.6 F., a pulse rate of 120 and a respiratory rate of 36. Recovery ensued in thirty-six hours. It is of interest that when he was profoundly affected, his respiratory rate was only 24, and later when his reaction was milder his respiratory rate was 36. This is an important criterion for the severity of an attack; the slower the respiratory rate, the greater the danger of asyphyxial death. We have observed this repeatedly in guinea pigs in anaphylaxis.

Park[17] reported a reaction to the egg allergen in typhus vaccine. The patient, a British airman aged 35, was admitted to the station hospital in collapse, vomiting blood and presenting asthmatic breathing and generalized urticaria. He soon became comatose. Symptomatic treatment resulted in complete recovery by the next morning. He had received an injection of typhus vaccine fifteen minutes before the described reaction occurred. He related that he had been allergic to egg all his life. His usual reaction to egg was vomiting or, if it did not occur, edema of the lips, tongue and larynx, asthma and urticaria would follow. Never before had he vomited blood or passed into coma. Skin tests were positive to egg proteins by the scratch method and also with passive transfer tests. Park reported that his patient had received an inoculation of yellow fever vaccine about a year previously without any ill effects. Apparently he was sensitive to the yolk allergen.

A case reported by Plotz[18] concerned a soldier who had received cholera and typhus vaccine at the same time. About

12. Cox, H. R.: Personal communication to the authors.
13. Eaton, M. D., and Meiklejohn, G.: Vaccination Against Influenza: A Study in California During the Epidemic of 1943-44, Am. J. Hyg. **42**: 28, 1945.
14. Sulzberger, M. B., and Asher, C.: Urticarial and Erythema Multiforme-Like Eruptions Following Injections of Yellow Fever Vaccine, U. S. Nav. M. Bull. **40**: 411, 1942.
15. Swartz, H. F.: Systemic Allergic Reaction Induced by Yellow Fever Vaccine, J. Lab. & Clin. Med. **28**: 1663, 1943.
16. Roth, V. E.: Reactions to Typhus Vaccine, Bull. U. S. Army M. Dept. 1945, No. 88, p. 111.
17. Park, R. G.: Allergy to Egg Prepared Vaccines, Brit. M. J. **2**: 570, 1945.
18. Plotz, H.: I. Skin Sensitivity Following the Subcutaneous Inoculation of Typhus Vaccines in Humans, J. Immunol. **53**: 315, 1946.

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ten minutes afterward, the patient had difficulty in breathing and almost immediately became cyanosed. Artificial respiration was given, but the patient died about thirty minutes after the administration of the vaccines. At autopsy, the lungs were found to be greatly distended, and they did not collapse on the opening of the chest cavity. The autopsy report was that of a typical guinea pig variety of anaphylactic death.

The case of Rubin [19] is of interest because a 19 year old soldier had a moderate allergic episode occurring one and one half hours after the inoculations of typhus fever and yellow fever vaccines. He attributed the reaction to an egg yolk sensitivity which this person had since childhood. Rubin showed conclusively that sensitivity to egg yolk was the dominant factor. This bears out the observations of Coulson and Stevens that although egg yolk and egg white have antigens common to both, they also have antigens independent of each other. The test results are of interest: egg white ±; egg yolk 4 plus; chicken meat 0; yellow fever vaccine 2 plus; typhus vaccine 4 plus. It should be recalled that yellow fever vaccine is made from chick embryo and typhus vaccine from egg yolk sac.

Plotz attempted a study to determine whether cutaneous sensitivity follows the subcutaneous inoculation of typhus vaccine in man. Skin tests were performed on 180 normal persons, as follows: (*a*) before inoculation with typhus vaccine; (*b*) one week after second subcutaneous dose of vaccine; (*c*) two weeks after third subcutaneous dose of vaccine, and (*d*) four weeks after third subcutaneous dose of vaccine. All persons who showed cutaneous sensitivity were again skin tested six, eight and twelve weeks after the course of three doses of vaccine, 1 cc. each, given subcutaneously on three successive weeks.

Only 1 of the 180 subjects tested before the administration of typhus vaccine gave positive reactions to all the skin test antigens employed (typhus vaccine, egg white and egg yolk). The reactions were moderate—3 cm. erythema and 1 cm. induration (wheal). This subject tolerated three weekly inoculations of 1 cc. each of typhus vaccine given subcutaneously without systemic reaction. In none of the subjects in the control group (skin tested, but not given injections of vaccine subcutaneously) did skin sensitivity develop. However, cutaneous sensitivity developed in 9 of 150 vaccinated subjects: 1, later, to egg yolk and egg white; 4 to vaccine alone; 2 to vaccine and egg yolk and 2 to vaccine, egg yolk and egg white. In all 9 cases, cutaneous sensitivity was noted four weeks after the third dose. The cutaneous sensitivity became negative after twelve weeks in 7 of the cases and diminished considerably in 2. In 2 persons the cutaneous reactions remained relatively unchanged twelve weeks after the third dose. These 2 subjects must have been sensitized to a greater degree than the others, for they reacted to egg yolk, egg white and vaccine. Despite the cutaneous sensitivity, all the subjects sustained a subsequent subcutaneous injection of the full dose of typhus vaccine without systemic reaction.

The suggestion of Beard, Finkelstein and Beard [20] that repeated vaccination with equine encephalomyelitis vaccine may sensitize man is provocative but not too clearly defined by their data. In 9 persons who were revaccinated, they observed symptoms of "crampy stiffness" and indefinite muscular soreness in the lower portion of the thigh. Local reactions were not present at the site of the injection. A test for sensitivity was not performed. Although allergic reactions can ensue from this vaccine, as attested to in studies with horses (Schoening, Wolfe and Trum and Graham) and in the guinea pig (van der Scheer and his associates), Beard and his co-workers are not justified in labeling as allergic the reactions they noted. As Coulson and Stevens point out equine encephalomyelitis vaccine is heavy, its absorption is slow, and the recorded symptoms may be caused by such factors, particularly in view of the large, 2 cc., dose injected. Allergy due directly to reinjection is an important matter, and further investigations should be undertaken to clarify this phase of the subject.

Two cases recounted to us are worthy of mention. Ira Rubin [21] recalled a case that he observed while in the army, of a man in his early twenties in whom asthma and generalized urticaria developed within five minutes after the injection of 1 cc. of influenza vaccine subcutaneously. The symptoms of asthmatic breathing and urticaria gradually disappeared after four days. Supportive and symptomatic therapy were administered. This patient gave a history of sensitivity to egg since childhood. One year prior to admission, he was given an injection of 1 cc. of typhus vaccine. Within fifteen minutes he was wheezing and had generalized urticaria. At that time he was also confined to the hospital for four days and received several injections of epinephrine. He was warned never to take any injection of a vaccine grown in an egg medium.

The second case was that of a woman a member of the Women's Army Corps, aged 25, who sustained a severe anaphylactic shock of a striking character. She was given 1 cc. of influenza vaccine at about 1 p. m. and was admitted to the hospital at 2 a. m. the following morning. Her blood pressure was 40 systolic and a questionable diastolic reading. She was treated for shock and was given epinephrine and ephedrine. Wheezing and urticaria were absent. The one sign was the tremendously lowered blood pressure. She was discharged in one week with a blood pressure of 80 systolic and 50 diastolic. A history of intolerance to egg was obtained. Although not all the data could be recalled, the striking situation here is that this patient in all probability suffered a canine type of anaphylactic reaction, the cardinal symptom of which is a fall in systemic blood pressure.

A study was undertaken by Stull [1] to determine whether vaccines grown on chick egg yolk sac contain sufficient egg proteins to cause severe systemic reactions if given to egg sensitive subjects. In this investigation, skin tests were not performed directly on egg sensitive patients because of the danger involved in possible production of systemic reactions. Serums from egg sensitive subjects were used, and the antigenic specificity and activity were shown by passive transfer. Prausnitz-Küstner reaction tests were performed on the skin of normal recipients.

These tests revealed the presence in egg embryo vaccines of egg white and yolk antigens of such quantity and specificity that their injection might produce dangerous systemic reactions in egg-sensitive recipients. Stull states that the recommended immunizing dose of typhus vaccine contains about two thousand times the dosage usually considered safe for intracutaneous skin tests in allergic subjects. He concluded from the result of his studies that if egg-sensitive persons were given injections of typhus vaccine similar to the lot used in his study, serious immediate systemic allergic reactions might ensue.

In a patient aged 33, Stull relates that a delayed allergic urticarial local reaction occurred seven days after the first injection of 1 cc. of equine encephalomyelitis vaccine (local serum sickness type of reaction [14]). Two weeks later a second injection of 1 cc. produced a large local reaction within one hour (accelerated reaction indicating allergy) which lasted for six days. Since that time this patient has had gastrointestinal disturbances with severe diarrhea following the eating of chicken or eggs. The serum of this recipient contained antibodies to egg yolk and chicken embryo but not to egg white.

Two additional cases were listed in the last *Quarterly Cumulative Index Medicus* by Sprague and Barnard,[22] who report alarming reactions in 2 patients at the time they received their original inoculation. One had been given yellow fever vaccine and the other typhus vaccine. After these episodes, a history of clinical sensitivity to egg was obtained in both. Skin tests performed later proved that they were sensitive to egg proteins and to the vaccines.

19. Rubin, S. S.: An Allergic Reaction Following Typhus Fever Vaccine and Yellow Fever Vaccine Due to Egg Yolk Sensitivity, J. Allergy **17**: 21, 1946.

20. Beard, D. W.; Finkelstein, H., and Beard, J. W.: Repeated Vaccination of Man Against Virus of Equine Encephalomyelitis, J. Immunol. **40**: 497, 1941.

21. Rubin, I.: Personal communication to the authors.

22. Sprague, H. B., and Barnard, J. H.: Egg Allergy: Significance in Typhus and Yellow Fever Immunization, U. S. Nav. M. Bull. **45**: 71, 1945.

HYPERSENSITIVITY REACTIONS TO INFLUENZA VACCINE, A AND B, IN ALLERGIC CHILDREN

All the cases used in the present study were those of children ranging in age from 1 to 18 years. These children were known to be allergic, were suffering from asthma, eczema, urticaria and hay fever and had been completely studied for their hypersensitivities. Each child had been tested against three hundred or more allergens. A case was not used unless the child had been under observation for several months to several years. For this reason, all these subjects were familiar to us not only through the knowledge of their protein cutaneous hypersensitivities but also through intimate knowledge of their clinical behavior toward egg and other proteins.

Those patients who reacted positively by scratch test to dry proteins (Arlington) of the egg-chicken family were regarded as positive reactors to egg. The patients whose reactions to the egg proteins were doubtful and who gave a history of intolerance to egg were further tested with egg white, egg yolk and chicken (1:500 dilution) by the intracutaneous method.

Methods and Procedures.—All subjects were given injections of 0.02 cc. of undiluted influenza A and B vaccine.[23]

TABLE 1.—*Positive Allergic Reactors to Influenza (Type A & B) Vaccine*

Case, Age	Allergic Diagnosis	Allergic Sensitiveness: To Other Than Egg Protein	Allergic Sensitiveness: To Egg White	Allergic Sensitiveness: To Related Egg Protein	Vaccine Reaction to Intradermal Injection (0.02 Cc.): Local	Vaccine Reaction to Intradermal Injection (0.02 Cc.): Systemic	Clinical Egg Sensitivity
1 D. D. 4-6	Eczema, Asthma, Hay fever, Urticaria	Inhalants, pollens, dust, bacteria	Moderate positive to intradermal (1:500); negative to scratch test	None	Definite wheal; erythema 4.0 cm.	None	Ingestion of egg precipitated allergic attacks, nausea
2 L. D. 9-6	Eczema, Asthma, Hay fever	Inhalants, pollens, dust, nuts, fish, bacteria, condiments	Large positive reaction to scratch test, 5 cm. wheal with surrounding erythema	Egg yolk ovovitellin (scratch test)	Large wheal 6.5 cm. with erythema	Severe asthmatic attack 2 hrs. after test; lasted through night	Sensitive to egg since infancy; cannot tolerate any food containing egg; causes attacks
3 E. D. 5-3	Asthma, Eczema, Hay fever	Inhalants, pollens, dust, peanuts, nuts, fish	Moderate positive only to intradermal test	None	Wheal and erythema 4.0 cm.	None	Cannot tolerate egg-containing foods
4 B. F. 3-1	Eczema	Inhalants, pollens, cocoa, vegetables, fish	Moderate positive to intradermal test	Egg yolk (scratch test)	Small wheal and erythema 3.0 cm.	None	Tolerates only hard boiled egg
5 W. F. 7-5	Eczema, Asthma, Hay fever	Inhalants, pollens, fish, nuts	Positive to scratch test	Egg yolk ovomucoid, duck egg, goose egg, chicken feathers	Positive moderate wheal and erythema 4.0 cm.	None	Has avoided egg for several years
6 B. H. 14-10	Eczema, Asthma, Hay fever, Urticaria	Inhalants, pollens, wheat	Positive only to intradermal (1:500)	None	Positive moderate wheal and erythema 3.5 cm.	None	Ten years ago, strongly positive to scratch test with egg white, yolk, ovomucoid, goose egg, duck egg; since then well immunized; eats egg and is regarded as tolerant to egg; reaction relates to residual skin sensitivity which sometimes remains for years
7 K. H. 9-1	Asthma	Inhalants, vegetables, chocolate, bacteria	Moderate positive only to intradermal	Suggestive reaction to yolk, chicken and feathers	Positive moderate wheal and erythema 3.5 cm.	None	Tolerates egg
8 M. H. 15-3	Asthma, Hay fever, Emphysema	Inhalants, pollens	Definite positive to scratch test	Ovomucoid, feathers	Moderate positive wheal and erythema, 4 cm.	None	Cannot tolerate egg or egg-containing foods
9 P. L. 6-0	Asthma, Hay fever	Inhalants, pollens, dust, nuts, fruit	Definite positive to scratch test	Egg yolk, ovomucoid, feathers	Strongly positive wheal (4 cm.) and surrounding erythema	Received 0.5 cc. subcutaneously following the intradermal reaction. An immediate reaction of generalized giant urticaria ensued which was followed by asthma; the generalized reaction persisted 2 days	Has been avoiding eggs since sensitivity was determined three years ago
10 R. S. 4-1	Asthma, Eczema	Inhalants, dust, pollens	Positive to scratch test and intradermal (1:20,000)	Yolk	Wheal (3.5 cm.) and surrounding erythema (1:10) dilution vaccine	None	History of exquisite sensitivity to egg; merest contact causes severe hives, angioneurotic edema, asthma and even stupor
11 B. W. 10-8	Eczema, Asthma, Hay fever, Urticaria	Inhalants, pollens, dust, milk, wheat, nuts, fish, vegetables, fruit	Positive only to intradermal (1:500)	None	Moderate positive wheal and erythema (3.0 cm.)	None	Ten years ago positive scratch test to egg white, yolk, ovomucoid; 4 years ago treated for egg intolerance; now eats egg and to all intents and purposes is nonsensitive at present

The tests were read immediately and at varying intervals up to one hour. A skin test was regarded as positive if the test revealed an erythema measuring at least 3 cm. in diameter and a wheal measuring at least 1 cm. or more.

23. This vaccine was supplied to us by Eli Lilly and Company, through the courtesy of Dr. Horace Powell, and is prepared in the following manner: Ten day incubated eggs are injected with influenza virus types A and B. Thus seeded, the eggs are further incubated for forty-eight hours, a large amount of virus developing in the allantoic fluid. By opening the embryo blood vessels, red blood corpuscles are allowed to mix in the embryonic fluids, which after they have been harvested and

(Footnote 23 continued on next page)

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Control tests were done at the same time with solution of formaldehyde, 1:2000, and merthiolate, 1:40,000 in isotonic solution of sodium chloride.

Whenever a suggestive or positive reaction was obtained with the influenza vaccine in patients who had previously been negative by scratch test to dry egg and chicken proteins, further control tests were made by intracutaneous injection of 0.02 cc. of egg white, 1:500, egg yolk, 1:500, and chicken, 1:500.

I. *Positive Allergic Reactors to Influenza (Type A and B) Vaccine*

Of a total of 108 allergic children, 11 reacted positively to a test with influenza vaccine (0.02 cc. administered intracutaneously). In table 1 can be seen the detailed evaluation of these cases. In every instance in which the vaccine test was positive, the child also reacted to egg white protein. There was not a single positive reaction to vaccine demonstrated in the face of a negative reaction to egg white. This affords proof, therefore, that the positive reaction to vaccine must be related in large measure or, indeed, entirely to the presence of egg white protein in the vaccine.

In none of the remaining 97 children was a positive reaction obtained to the vaccine in the absence of a positive reaction to egg white.

In cases 2 (L. D.), and 9 (P. L.), systemic allergic reactions were induced by the injection of influenza vaccine. In the first instance, a large local reaction ensued, followed two hours later by an attack of asthma which persisted through the night. This was the only one of the 11 cases of sensitivity to egg white in which a systemic reaction developed from the small intradermal test dose of 0.02 cc. The child was known to be decidedly sensitive to egg white.

In the second case, in which the clinical and dermal sensitivity of the patient were less pronounced one-half hour after the intradermal test, which provoked a large local reaction but not a general reaction, a dose of 0.5 cc. of the vaccine was administered subcutaneously with due precaution and with epinephrine at hand. A generalized reaction occurred after this larger subcutaneous injection.

In cases 5 (W. F.) and 8 (M. H.) both patients reacted definitely to the scratch test with egg white vaccine and related egg proteins. These patients should be regarded as highly sensitive. In case 10 (R. S.), that of a girl who has had profound clinical allergic reactions from contact with egg, even to touch, an attempt to test with the full strength of the test materials was not made. She should be regarded as potentially exquisitely sensitive and perhaps would show a systemic reaction to the test in full strength.

Cases 6 (B. H.) and 11 (B. W.), are those of 2 children who ten years prior to this study were known to be extremely sensitive to egg white. Over a period of years both children were given egg white in gradually increasing doses, and both have tolerated egg in regular amounts in their diets for about eight years. Skin tests with egg white show that the two have only a residual dermal sensitivity to egg by the scratch test and only a moderately positive response by the intradermal route. The vaccine reaction was only moderate in degree. In the same category of moderate sensitivity, with probable absence of systemic reaction, can be placed cases 1 (D. D.), 3 (E. D.), 4 (B. F.), and 7 (K. H.); these patients did not react to the scratch tests and reacted only moderately to the intracutaneous (1:500 dilution) and moderately to the vaccine test.

II. *Suggestive Allergic Reactors to Influenza (Type A and B) Vaccine*

In this group of 39 patients, a doubtful reaction was obtained to the vaccine test dose. By doubtful we mean that there was not a definite wheal, and the erythema measured about 2 cm. Ten of these patients, all proved to be allergic when studied from the standpoint of other proteins to which they were found sensitive, gave suggestive reactions to various egg proteins. None of them could be regarded as clinically sensitive to egg.

TABLE 2.—*Types of Reactions to Virus and Rickettsial Vaccines*

	Allergic	Nonallergic; General
1. Onset	Sudden and explosive	Delayed
2. Fever	Absent	Moderate
3. Chills	Absent	Present
4. Local skin reaction to vaccine	Prompt whealing or persistent erythema	Usually absent; when present, delayed, redness and swelling
5. Local skin reaction to egg proteins	Present, usually egg white	Absent
6. Allergic manifestations	Various forms, usually urticaria, asthma and others	Absent
7. History of allergy to egg	Often present	Usually absent
8. Clinical hypersensitivity to egg or chicken proteins	Usually present	Absent
9. History of allergy to other substances	May be present	May be present
10. Eosinophilia	Often present	Usually absent

For example, of the 10 patients, 6 gave positive reactions to ovomucoid; of these 6, 3 showed suggestive reactions to other egg proteins, including egg white. Of the remaining 4, 1 reacted suggestively to egg yolk alone, 1 to egg yolk and egg white, 1 to egg white alone and 1 to chicken, egg yolk and egg white. None of these children gave a clinical story of sensitivity to egg.

Three children aged 7, 8 and 11 gave a history of intolerance to egg but demonstrated not even a suggestive reaction to egg protein. It is more difficult to explain the suggestive reaction to the vaccine in these cases, for the clinical sensitivity must have worn off entirely.

In the remaining 26 of this group that had a suggestive reaction to the vaccine, neither the egg test nor the history was positive. One cannot consider these reactions related to sensitivity to egg.

It must be assumed, therefore, that suggestive reactions to the vaccine are in some instances related to moderate sensitivity to egg and in other instances to sensitivity to some other ingredient in the vaccine mixture. In 4 instances, the reaction was just as large to the injection of solution of formaldehyde in the dilution of 1:2000 as it was to the vaccine.

pooled, are subjected to lowered temperatures. The virus, adsorbed to the red blood cells, is separated from the fluid by cold agglutination of the red blood cells, then allowed to elute under raised temperature. After centrifugation, the supernatant fluid contains active virus, suspended in isotonic solution of sodium chloride and concentrated to ten times the original virus concentration of the incubated egg fluids. Inactivation is effected with addition of solution of formaldehyde 1:2000, and preservation with merthiolate 1:40,000.

We lack evidence in these studies that these children could tolerate the full dose of vaccine. We have every right to assume that they would not react adversely to such an injection. This phase will be the subject of a future publication.

In a parallel series of 28 normal children who did not present evidence of allergy in any form 8 also gave suggestive reactions to the vaccine, which reaction must be attributed to some nonspecific irritant or to a possible sensitivity to the solution of formaldehyde.

Whether sensitivity to influenza virus does exist is not known. It would appear for the present that only reactions to egg proteins are responsible for the positive reaction.

III. *Negative Reactors to Influenza (Type A and B) Vaccine*

This group of negative reactors to influenza (type A and B) vaccine comprises the largest number, totaling 59 cases. These children, as did those in the preceding group, all suffered from one or more of the cardinal allergic diseases; all were thoroughly studied and reacted to allergens other than egg.

Five children in this group gave suggestive reactions to egg proteins; 3, to proteins other than egg white, such as ovomucoid, ovovitellin and egg yolk; and 3, to egg white: 1 to egg white and ovovitellin, 1 to egg white and egg yolk and 1 to egg white alone. None of these children reacted to influenza vaccine; hence they must be regarded as so insignificantly sensitive to egg white as not to react to the vaccine. The remaining 54 children were negative throughout.

COMMENT

There are apparently two types of reactions that may ensue from the administration of virus or rickettsial vaccines. The first are the general constitutional reactions characterized by moderate fever, chills, malaise and delayed onset of symptoms. They occur in persons who may or may not have a personal history of allergy and who do not show eosinophilia. These reactions can vaguely be explained on the basis of reaction to a foreign protein.

The second type, with which we are here concerned, are the allergic reactions characterized by lack of fever, by immediate or explosive onset and by one or more of the varying allergic manifestations, such as asthma, gastrointestinal symptoms, angioneurotic edema, urticaria and other rashes. These patients often have an eosinophilia and a history of allergy to egg (see table 2).

Our study suggests that the positive allergic reaction to vaccine must be related in large measure, if not entirely, to the presence of egg white protein in the vaccine, for never was a positive reaction to the vaccine obtained in the absence of a positive reaction to egg white.

From a review of the literature there is little doubt that immediate, profound and even fatal reactions may ensue from the first injection of vaccine in a person exquisitely sensitive to egg white. In such cases our observations show that an intradermal inoculation of 0.02 cc. of the vaccine used as a preliminary test may induce a systemic allergic response. This is exemplified by case 2 (L. D.). It is imperative when a person reacts to the preliminary intradermal test in this manner that further administration of vaccine be withheld. Such instances are rare, however.

In case 9 (P. L.), although a large local, without a systemic, reaction resulted from administration of the test dose (0.02 cc.), when a larger dose (0.5 cc.) was administered subcutaneously one-half hour later, a profound generalized allergic reaction occurred. A large local positive intradermal reaction is evidence, therefore, for the need of exercising caution in the prophylactic administration of the vaccine. Further attempts to gather additional data on this point were not made because of the danger inherent in such a procedure.

When a local reaction is moderate in size, Plotz [18] has shown that the subsequent administration of three weekly inoculations of 1 cc. each of typhus vaccine can be tolerated without systemic reactions. This observation is fortified by cases 6 (B. H.) and 11 (B. W.) in our series; ten years previously these patients were decidedly sensitive to egg white, while at present only a moderate local reaction was obtained, indicating a waning sensitivity. It is reasonable to assume that this type of patient can tolerate a full prophylactic dose of vaccine.

Although related egg proteins apparently play a negligible role in this type of vaccine hypersensitivity, in all instances in which great sensitivity to egg white was evident, related sensitivity to egg protein was also present. This did not hold with equal regularity in instances in which there was residual or moderate sensitivity to egg, in most of which related sensitivity to egg protein was absent.

Of the 11 patients sensitive to egg white and vaccine, only 5 (cases 2, 5, 8, 9 and 10) could be regarded as sensitive enough to make circumspection and caution necessary in the use of the vaccine. Therefore, even though 11 of 108 patients (10.2 per cent) were sensitive to the vaccine, it appears that only 5 (4.6 per cent) were sensitive enough to warrant caution in administering the vaccine. Given an allergic group of children, one might therefore expect about 5 per cent to be sensitive enough to egg white to be decidedly sensitive to the vaccine. If the incidence of allergy in the general population is 10 per cent, then the serious egg allergenicity in the general population would be 5 per cent of 10 per cent (0.5 per cent or 1 in every 200 persons). If sensitivity to egg is more prevalent among children, as are all food sensitivities, then the figure of 0.5 per cent in the general population can be further reduced. This is in accord with the point of view of Plotz.

In order to safeguard these seriously sensitive persons, 1 or fewer in every 200 who are to receive vaccine, it is not alone sufficient to obtain a history of allergy to egg, for often this is vague, but a test dose of vaccine should be given before each and every prophylactic injection and perhaps also a test should be made with egg white. If both or either is strongly positive, the patient is seriously sensitive, and vaccine should be withheld. If a systemic reaction results from the test dose, vaccine should be withheld unconditionally. If only a moderate local reaction ensues, the vaccine can be given in three to six divided doses, spaced at one, two or three day intervals, with the concomitant administration of epinephrine (3 minims [0.18 cc.] of a 1:1000 dilution). These phases will be the subject of further investigation.

The 39 patients who gave only suggestive reactions to the vaccines also gave suggestive reactions to one or more of the egg proteins. These children for the most part were from 8 to 13 years of age and in all probability had a moderate or mild sensitivity, which at

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present is not of clinical significance. In a number of instances, some of these suggestive reactors were shown to be sensitive to the solution of formaldehyde and not to egg.

Lt. Col. Johnson F. Hammond, M. C.,[24] has stated: "Several severe reactions have been reported to the Surgeon General's office. The number of reactions known to have occurred is negligible in comparison with the number of doses of egg vaccine administered, now in the millions. Nevertheless, medical officers should be alert to the possibility of egg sensitivity in persons given typhus vaccine, yellow fever vaccine, or other prophylactic biologicals derived from eggs. If individuals suspected of being egg sensitive are given skin tests to confirm the diagnosis, egg vaccine material should be diluted 1000 fold and intradermal skin tests done by the injection of as small an amount as possible. If this test is negative, it may be repeated with a 1 : 100 dilution and should this be negative, with a 1 : 10 dilution. Undiluted vaccine may produce nonspecific irritative skin reactions. Desensitization is not recommended."

Several of the authors reviewed herein have expressed the opinion that the incidence of sensitivity in the army experience is smaller than it would be in civilian practice, particularly among children. It was with this in mind that the present study was undertaken in this highly potential group.

We believe that a history of allergy per se is not of any significance whatsoever, for allergic persons without specific sensitivity to egg proteins are not more likely to have a reaction from vaccine than is a nonallergic person. We are further of the opinion that a history of sensitivity to egg is of questionable value since in case 9 the patient who was highly sensitive to egg white, had a constitutional reaction to the injection of vaccine. When first studied by us for his allergy two years previously, the disclosure of sensitivity to egg was a complete surprise to his parents.

We agree with Colonel Hammond that all precautions should be taken before each and every administration of vaccine. From our experience we should like to offer certain suggestions and draw the following conclusions:

CONCLUSIONS

1. In a group comprising 108 highly allergic children who were studied completely for their allergy, 10.2 per cent were sensitive to eggwhite protein. However, only 4.6 per cent were sensitive enough to be regarded potential hazards for influenza vaccine administration.

2. Untested patients have been known to have a profound or fatal anaphylaxis from a first or subsequent prophylactic injection of influenza vaccine.

3. All persons should be tested intradermally with undiluted vaccine, using 0.02 cc. before administering each and every prophylactic dose.

4. If the test dose is negative or suggestive, the vaccine can be given with impunity.

5. If a moderate local reaction ensues, the vaccine can be administered with the added precaution of using 2 or 3 minims (0.12 to 0.18 cc.) of epinephrine simultaneously.

6. If a large local reaction is obtained, the vaccine can be given with the added precautions of using epinephrine just prior to the administration and giving the vaccine in divided doses at one, two or three day intervals. The vaccine can also be tried intradermally in several repeated doses of one-tenth the required amount. If this proves immunologically adequate, it may be the method of choice.[25]

7. If a test dose induces a systemic reaction, the vaccine should be withheld unconditionally.

8. Attempts should be made to rid the vaccine of as much egg protein as is possible in its manufacture.

9. A history of sensitivity to egg is not as reliable a criterion as an intradermal test with the vaccine.

10. Egg protein skin tests are necessary only for academic or research purposes, for it is proved by other observations, as well as by our own, that allergic vaccine reactions of any consequence are due entirely to the egg protein content of the vaccine.

11. Use of a virus or rickettsial vaccine for prophylaxis need not be feared if the single admonition is observed of preceding each and every prophylactic injection with an intradermal test dose of vaccine. This simple measure eliminates practically all hazard from the vaccine's use in the persons, approximately 0.5 per cent of the general population, who are hypersensitive to egg.

12. Use of vaccines is not dangerous to 99.5 per cent of the general population, which includes all the allergic persons who are sensitive to proteins other than egg and about 50 per cent of the persons moderately sensitive to egg. With further purification of the vaccine, even this small hazard can be further reduced.

13. The virus and rickettsial vaccines should be used with increased frequency in the civilian population, but the simple precautions herein outlined should be meticulously observed, to eliminate most, if not all, risk to the egg-sensitive person.

50 East Seventy-Eighth Street.

24. Hammond, J. F., cited by Roth.[18]

25. Ratner, B.: Allergy, Anaphylaxis and Immunotherapy, Baltimore, Williams & Wilkins Company, 1[illegible]

Prognosis in Coronary Disease.—Coronary disease persisted more than twenty years in 11 of my patients, more than thirty years in 2 of them. The record duration was fifty-two years in a lady who had her first attack of angina at the age of 30; she was leading a busy life at the age of 80, though still liable to angina whenever she walked. She died suddenly at the age of 82. It has long been known that quite extensive coronary disease is compatible with an active life and need not necessarily be associated with angina. In fact this used to be put forward as an argument against the view that angina is due to coronary ischemia. Coronary occlusion often antedates angina. It did so in 225 (22.5 per cent) of my cases. Yet before coronary occlusion can occur there must almost always be coronary disease. Moreover, a remarkably complete functional recovery is possible after a coronary occlusion. One of my patients played vigorous games after a coronary occlusion at the age of 39. He had a second attack at the age of 48 and, against advice, was playing tennis regularly two years later without any angina. Now at the age of 58 he is at work, plays golf and mows his lawn without cardiac symptoms. It is common for coronary disease to be entirely latent till sudden death takes place. Professor Hume of Newcastle tells me that since 1911 he has performed or attended postmortem examinations on 160 miners who had died suddenly and unexpectedly in the pit or in close proximity to it. The cause of death in each instance was coronary atheroma, and most of the men had been working regularly, without complaint, up to the moment of their fatal collapse. Only 40 had premonitory symptoms—Cassidy, Sir Maurice: Coronary Disease, *Lancet*, Oct. 26, 1946.

FOLIC ACID IN THE REHABILITATION OF PERSONS WITH SPRUE

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The observations of Spies and associates from studies made in the Calixto Garcia Hospital, Havana, Cuba, and carried out under the auspices of the University of Cincinnati, the University of Havana and the Institute of Nutrition of Cuba have made it abundantly clear that persons with sprue in relapse are profoundly benefited by the administration of synthetic folic acid. The acute manifestations of the disease subsided rapidly as the blood began its regeneration, and the alimentary tract tended to regain its normal function.[1] Although these cooperative studies are still in progress, we already

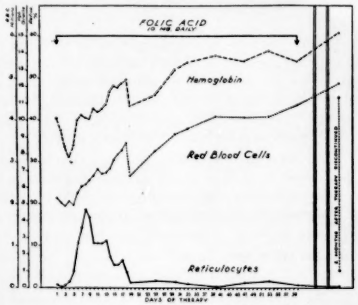

Fig. 1 (case 6).—Effect of folic acid on macrocytic anemia of sprue.

have seen persons with sprue rehabilitated by means of folic acid therapy. The present report is confined to this aspect of our studies in 18 cases of sprue. The acute manifestations and the early response to folic acid in 9 of these cases have been reported.[1a] The present report includes and extends our observations in those 9 cases and includes 9 additional cases.

Eighteen patients were selected for study using the following criteria: 1. The patient must have macrocytic anemia. 2. The bone marrow must show the typical erythroblastic arrest seen in pernicious anemia. 3. The erythrocyte counts must be below 2.5 million. 4. The patient must be untreated, or he must not have been treated recently enough to interfere with our evaluation of the effect of folic acid. 5. He must have persistently low reticulocyte counts during the period of observation. 6. He must have glossitis and diarrhea characterized by fatty stools.

Fig. 2 (case 6).—*A*, liquid character of the stools on the day of admission to the hospital; *B*, stool seventy-two hours after the initiation of folic acid therapy.

Each patient selected was admitted to the hospital for preliminary examination, base line determinations and treatment in which the following plan of study was observed: From the time the patients were admitted their diets were rigidly controlled. Meat, meat products, fish and poultry were excluded, and only 1 quart

Fig. 3 (case 6).—Bilateral edema; note area of pitting on the right ankle following pressure with thumb.

of milk and 1 egg were allowed daily. All other foods were allowed to the extent desired. In each case a detailed medical and dietary history was obtained and a careful physical examination made. Daily hematologic examinations included white and erythrocyte

The folic acid was supplied by Lederle Laboratories, Inc.
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University of Cincinnati Studies in Nutrition at the Calixto Garcia Hospital, Havana, Cuba, in cooperation with the Institute of Nutrition of Cuba and the University of Havana.
In the medical care of the patients included in this study we were assisted by many physicians who voluntarily aided us throughout the course of the study. In the special nursing and dietary care of the patients we were assisted by Miss Mariana de la Fuente, Miss Maria del Carmen Gonzalez, Miss Flora Villate, Miss Angela Pedraza, Miss Maria de las Angeles Perez, Miss Eva Averoff, Mrs. Eleanor Bennett and Miss Monette Springer, nurses, and by Mrs. Myrtle Neblett and Miss Jean Grant, nutritionists. The hematologic examinations were made by Mrs. Mary B. Koch, Miss Virginia Minnich and Miss Georgia Gwinner.

1. (*a*) Spies, T. D.; Milanes, F.; Menendez, A., and Minnich, V.: Observations on the Treatment of Tropical Sprue with Folic Acid, J. Lab. & Clin. Med. **30**: 1036, 1945. (*b*) Spies, T. D.: Effect of Folic Acid on Persons with Macrocytic Anemia in Relapse, J. A. M. A. **130**: 474 (Feb. 23) 1946.

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blood cell counts, hemoglobin determinations and reticulocyte counts. (Certified Trenner pipets were used for both the white and erythrocyte blood cell counts.) The hemoglobin content of the blood was determined in grams by means of a Leitz colorimeter, and the reticulocytes were counted in wet preparations by the use of a modified brilliant cresyl blue solution of Dameshek. From time to time cell volumes were determined on oxalated venous blood by means of Wintrobe hematocrit tubes. In each case bone marrow was obtained prior to treatment by sternal aspiration. Differential counts were made on preparations stained with both supravital and Wright-Giemsa stains. Gastric contents were collected before and after injections of histamine. Twenty-four hour stool specimens were collected daily in a single large glass graduated container. The stools were examined every day for appearance and volume. Each patient was questioned every morning concerning the number of bowel movements. Examination of the feces included tests for acidity, fatty acid determinations by the method of Labbe and Larue, bacteriologic examinations and examinations for parasites. Serum protein determinations were made in each case. In

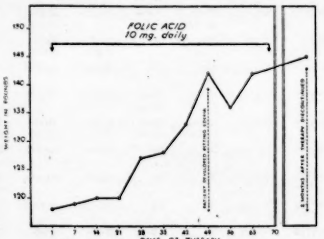

Fig. 4 (case 6).—Gain in weight by patient with sprue.

most cases blood calcium, phosphorus, potassium, amylase and lipase determinations were made.

After base line determinations were obtained, folic acid was administered orally in water suspension between meals. It was prepared by mixing it to a smooth paste with 4 or 5 drops of cold water and then adding 20 cc. of cold water while the mixture was being stirred constantly. After the patient drank this material, a small amount of water was used to rinse the glass thoroughly, and he drank this also to insure his getting as much of the folic acid as possible. During the latter part of the study folic acid became available in tablets, and it was administered in this form. In the first cases studied (cases 1, 2, 5, 7, 8, 9 and 11) when we knew little about dosage, 100 mg. was administered twice daily. Subsequently, the dosage in these cases was reduced to 100 mg. daily and then to 25 mg. daily. From cases studied later (cases 3, 4, 6, 10, 12, 13, 14, 15, 16, 17 and 18) we learned that 5 to 10 mg. daily is just about as effective as the larger doses.

Dietary histories revealed that in every instance the dietary had not been completely adequate even prior to the onset of illness. The foods conspicuously lacking or eaten in insufficient amounts were meat, fish, poultry, eggs and milk. In all cases cereal foods, root vegetables and dried beans had been the foods used most commonly and in the most liberal amounts. Following the onset of illness, loss of appetite and soreness of the tongue had so interfered with the intake of food that in each case the diet of the patient was grossly deficient in all nutrients.

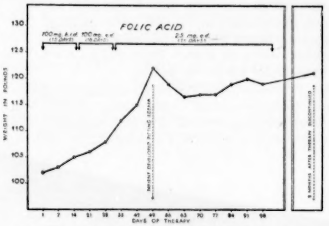

Fig. 5 (case 8).—Gain in weight by patient with sprue.

The major clinical symptoms on admission are shown in table 1.

The hematologic observations before and after therapy are shown in table 2. Many of the laboratory studies are still in progress. A complete report of determinations on bone marrows and stools subsequent to folic acid therapy will be published later. Suffice it to say at this time that both the bone marrow and stool determinations tend to revert to normal.

The typical clinical and hematologic response to therapy and the complete rehabilitation following therapy are illustrated in the following cases:

REPORT OF CASES

CASE 6.—*History.*—A. M., a white man aged 37, was admitted to the General Calixto Garcia Hospital on Nov. 30, 1945, with a history of loss of appetite, diarrhea, weakness, dizziness and soreness of the mouth and tongue of one year's duration. The family history and past history were noncontributory.

Until one year prior to his admission he had worked strenuously as a wood-cutter. He had a good appetite and ate large amounts of rice, dried beans and root vegetables. He disliked fruit and fresh vegetables and never ate them, and he seldom ate eggs or meat or drank milk. One year prior to his admission he began having severe diarrhea, which persisted for two

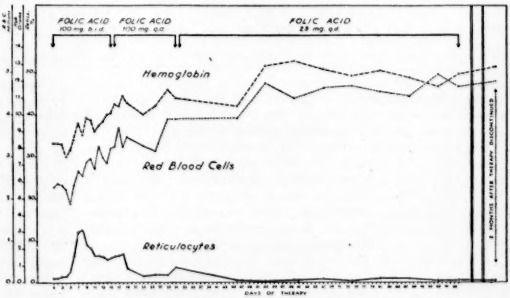

Fig. 6 (case 8).—The effect of folic acid on macrocytic anemia with sprue.

weeks. During this time he had anorexia, weakness and loss of weight and was unable to work. His physician prescribed emetine, and the diarrhea disappeared. Although there was little improvement in his appetite or strength following the cessation of the diarrhea, he returned to work and continued to work for four months, at the end of which time he again

began having diarrhea. This time emetine failed to give relief. He had from four to six voluminous, foul-smelling, liquid or semisolid, yellow foamy stools a day which were accompanied by a sensation of flatulence and severe burning of the rectum. Since he did not desire food and thought that it aggravated his diarrhea, he restricted his diet to rice, bread and coffee. A few days after the diarrhea began he observed that his tongue was red and sore. A few weeks later he began having pain and paresthesias in the lower extremities. He grew progressively weaker, and for two weeks prior to his admission he had been unable to work. During the year he was ill he lost 32 pounds (14.5 Kg.) in weight.

Physical Examination.—Physical examination showed a well developed, undernourished, pale, weak, listless man who appeared extremely depressed. The skin was pale and generally dry and pigmented over the anterior surface of both legs. The tongue was slick except for many hyperemic papillae along the edges. The peripheral reflexes of the legs were uniformly diminished. The remainder of the physical and neurologic examinations revealed essentially normal conditions.

Laboratory Data.—Blood: Examination of the blood revealed the following: red blood cells, 2.13 million; hemoglobin, 10.1 Gm. (66 per cent) per hundred cubic centimeters; white blood cells, 5,200, and reticulocytes, 0.8 per cent. The mean corpuscular volume was 131 cubic microns, the mean corpuscular hemoglobin was 47 micromicrograms and the mean corpuscular hemoglobin concentration was 36 per cent.

Differential Bone Marrow Counts: In the bone marrow the percentage of cells was as follows: metamyelocytes, 17.0; myelocytes C, 13.5; myelocytes B, 1.5; band neutrocytes, 5.0; segmented neutrocytes, 30.0; basophils, none; eosinophils, 6.0; megakaryocytes and plasma cells, none; lymphocytes, 23.5; clasmatocytes, 3.5, and reticulum cells, none, for a total of 100 per cent. The number of megaloblasts was 3; early erythroblasts, 17; late erythroblasts, 35, and normoblasts, 79.

Gastric Analysis: A fasting specimen of the stomach contents gave a determination of 40 degrees free hydrochloric acid and 50 degrees total acidity. The reading thirty minutes after histamine stimulation was 95 degrees free hydrochloric acid and 100 degrees total acidity.

Serum Protein: The determination of serum proteins was: total, 5 Gm.; albumin, 2.2 Gm.; and globulin, 2.4 Gm., per hundred cubic centimeters. The serum cholesterol reached a total of 203 mg. and the serum cholesterol ester, 128 mg., per hundred cubic centimeters. Other determinations were: calcium, 12.0 mg.; phosphorus, 3.5 mg., and potassium, 10.0 mg., per hundred cubic centimeters. The serum amylase level was 110 units, the serum lipase, 0.3 (cc. of twentieth-normal sodium hydroxide per hundred cubic centimeters).

Stool Examination: Stool examination showed Trichuris trichiura, Necator americanus and Giardia intestinalis. Pathogenic bacteria were not obtained on culture.

Proctoscopic Examination: Proctoscopic examination showed normal mucosa without ulceration.

TABLE 1.—*Major Clinical*

Case	Patient	Age	Sex	Duration of Present Illness	Loss of Appetite	Weight Loss		Weakness	Dizziness	Headache	Sore Tongue	Glossitis	Nausea	Vomiting	Burning of Stomach	Epigastric Distress	Flatulence
						Lb.	Kg.										
1	C. G.	29	♀	10 mos.	Yes	25	11.3	Extreme	Yes	Frequent	Severe	Severe	Occasional	No	Severe	Severe	Yes
2	M. S.	46	♀	1 yr.	Yes	47	21.3	Extreme	Yes	Occasional	Severe	Severe	Frequent	Frequent	Severe	Severe	Yes
3	C. B.	47	♀	6 mos.	Yes	15	6.8	Extreme	Yes	Occasional	Severe	Severe	Occasional	Occasional	Severe	Moderate	Yes
4	J. C.	63	♂	8 mos.	Yes	18	8.2	Moderate	Yes	No	Moderate	Moderate	No	No	Moderate	Moderate	Yes
5	G. A.	62	♂	1 yr.	Yes	30	13.6	Extreme	Yes	Frequent	Severe	Severe	No	No	Severe	Severe	Yes
6	A. M.	37	♂	1 yr.	Yes	32	14.5	Extreme	Yes	No	Severe	Severe	Occasional	Occasional	Severe	Severe	Yes
7	A. F.	75	♂	6 mos.	Yes	58	26.3	Extreme	No	No	Severe	Severe	Occasional	Occasional	Moderate	Moderate	Moderate
8	P. E.	63	♂	5 yrs.	Yes	20	9.1	Extreme	Yes	Frequent	Severe	Severe	No	No	Severe	Severe	Severe
9	J. G.	40	♂	5 yrs.	Yes	27	12.2	Extreme	Yes	Almost constant	Severe	Severe	No	No	Severe	Severe	Moderate
10	D. L.	67	♀	1 yr.	Yes	30	13.6	Extreme	No	Frequent	Severe	Severe	No	No	Severe	Severe	Moderate
11	F. G.	33	♀	2 yrs.	Yes	16	7.3	Extreme	Yes	Frequent	Severe	Severe	No	No	Moderate	Moderate	Moderate
12	R. C.	43	♂	5 yrs.	Yes	25	11.3	Moderate	Yes	Occasional	Moderate	Moderate	No	No	Moderate	Moderate	Moderate
13	I. D.	64	♂	7 yrs.	Yes	17	7.7	Extreme	Yes	No	Moderate	Mild	No	No	No	Occasional	Yes
14	C. C.	44	♂	1 mo.	Yes	20	9.1	Extreme	Yes	Seldom	Severe	Severe	No	No	Moderate	Moderate	Severe
15	F. S.	75	♂	5 yrs.	Yes	40	18.1	Extreme	Yes	Occasional	Occasional	Moderate	No	No	No	At times moderate	Moderate
16	E. E.	75	♂	5 yrs.	Yes	36	16.3	Extreme	Yes	Severe	Severe	Yes	No	No	No	Moderate	Severe
17	F. P.	66	♂	?	Yes	34	15.4	Extreme	Yes	No	Severe	Severe	No	No	At times severe	At times severe	Severe
18	E. V.	23	♂	9 mos.	Yes	32	14.5	Extreme	Yes	No	Severe	Yes	Occasional	Occasional	Severe	Severe	Severe

Progress.—On admission to the hospital the patient was given the diet previously described. After the base line studies were completed, he was given 10 mg. of folic acid a day by mouth. On the fifth day of therapy the reticulocytes rose to 4.0 per cent and reached a peak of 18.8 per cent on the eighth day. By the fourteenth day the red blood cells had increased to 2.84 million and the hemoglobin to 11.7 Gm. (76 per cent). At the time the patient was discharged, sixty-six days after folic acid therapy was initiated, the red blood cell count was 4.36 million, the hemoglobin 13.5 Gm. (88 per cent) and the reticulocytes 0.8 per cent. See figure 1 which shows the hemopoietic response.

The clinical improvement paralleled the hemopoietic response. Three days after therapy was initiated the patient stated that he felt stronger and said that he was hungry. He took all the food he was offered and asked for additional servings, whereas prior to treatment he usually refused everything on his tray except soup and coffee. Two days later he volunteered the information that his mouth and tongue no longer burned. A striking decrease in the diarrhea likewise occurred on the third day of therapy. That day he had only two stools which were soft, rather liquid, normal in color and not foamy (fig. 2).

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Rectal burning ceased, as did the sensation of flatulence. Between the forty-second and forty-ninth days of treatment pitting edema of the ankles appeared (see fig. 3), then subsided the following week. This clinical and hematologic improvement occurred despite the fact that he was not given antiparasitic therapy; examination of his stools subsequent to the administration of folic acid showed the presence of all the parasites found prior to treatment. By the time he was discharged on the sixty-sixth day of therapy he had gained 27 pounds (12 Kg.) (see fig. 4). The day after he was discharged he returned to work as a wood-cutter. Two months later he returned for follow-up studies. At this time he was in excellent health. He was eating regularly the recommended diet which included liberal amounts of meat, eggs and milk. Bowel movements were occurring only once a day and were normal in volume, consistency and color. Although he had worked strenuously six days a week he had gained 3 pounds (1.4 Kg.). Examination of the blood showed red blood cells, 4.87 million; hemoglobin, 15.2 Gm. (99 per cent), and reticulocytes, 0.4 per cent.

Symptoms on Admission

No. of Stools in 24 Hrs.	Bulky Stools	Consistency of Stools	Foamy Stools	Color of Stools	Blood in Stools	Mucus in Stools	Bowel Movement Accompanied with Colic	Rectal Burning on Defecation	Time of Severity of Diarrhea	Diarrhea Aggravated by Food	Pain in Extremities	Paresthesias	Pitting Edema
10-12	Yes	Watery	Yes	Yellow	No	No	Yes	No	After meals	Yes	Yes	Yes	Yes
10 or more	Yes	Semiliquid	Yes	Yellow	No	No	Occasional	No	After meals	Yes	Yes	Yes	Yes
14-18	Yes	Semiliquid	Yes	Yellow	No	Occasional	Yes	Yes	After meals	Yes	No	Yes	Yes
3-4	Yes	Semiliquid	Yes	Light	No	No	Yes	No	After meals	Yes	No	Yes	No
15-16	Yes	Watery	Yes	Yellow	No	Occasional	Yes	No	All hours; no particular time	No	No	Yes	Yes
4-6	Yes	Watery	Yes	Yellow	No	No	Yes	Yes	Evening	No	Yes	Yes	Yes
7-8	Yes	Watery	Yes	Yellow	No	No	No	No	During night	No	Yes	No	Yes
20-30	Yes	Watery	Yes	Greenish yellow	No	No	Severe	No	All hours; no particular time	No	Yes	Yes	No
5-6	Yes	Watery	Yes	Greenish yellow	No	Yes	Severe	Yes	Morning	Yes	Yes	Yes	Yes
2-3	Moderately	Watery	Yes	Yellow	No	Occasional	Occasionally moderate	Yes	After meals	Yes	Yes	Yes	Yes
3-4	Yes	Watery	Yes	Yellow	No	No	Rarely	No	During night	No	Yes	Yes	Yes
15-17	Moderately	Watery	Yes	Light brown	Yes	Yes	Occasional	No	Morning	Yes	No	Occasional	No
15-20	Yes	Watery	Yes	Whitish yellow	No	No	Yes	No	Morning	Yes	Yes	Yes	Yes
7-8	Yes	Watery	Yes	Yellow	No	No	Yes	Yes	No particular time	No	Yes	Occasional	Yes
4-5	Yes	Mushy	Occasional	Light brown or yellow	No	Occasional	Yes	No	After lunch	Yes	Yes	Severe	Yes
6-8	Yes	Watery	Yes	Light	Yes	No	Yes	Yes	No particular time	No	Yes	Yes	No
10-14	Yes	Semiliquid	Yes	Yellow	No	No	Yes	Yes	During night	No	Yes	No	Yes
6-8	Yes	Liquid	Yes	Yellow	No	No	Yes	Yes	Evening	Yes	Yes	No	No

CASE 8.—*History.*—P. E., a white man aged 63, was admitted to the General Calixto Garcia Hospital on Nov. 19, 1945, with a history of diarrhea, loss of appetite, weakness and burning of the mouth and tongue of five years' duration. The family history and past history were noncontributory.

For a number of years his diet had consisted chiefly of potatoes, root vegetables, corn in various forms and from three to four eggs daily. He rarely drank milk and seldom ate beef and pork because he thought they caused gastric distress. Other than occasional gastric distress following the ingestion of beef and pork, his health had been perfect until five years before admission to the hospital, when he noticed a burning sensation of the mouth and tongue. Soon after this he began to have severe diarrhea. Sometimes he had thirty bowel movements a day which were usually preceded by severe colic. The stools were yellow in color and foamy. He consulted a physician who prescribed liver extract, which he took intermittently for three years, during which time he remained well. One and one-half years after he discontinued taking liver extract he again began to have diarrhea, and all the symptoms he had during his first illness reappeared. He lost his appetite, began having paresthesias of the legs, dizziness and tinnitus, and he became progressively weaker. After losing 20 pounds (9 Kg.) he reported to his physician, who sent him to us.

Physical Examination.—Physical examination showed a well developed, pale, emaciated man who lay quietly in bed without apparent desire to move. The tongue was slick and shiny and was intensely red along the tip and edges. The remainder of the physical and neurologic examination revealed essentially normal conditions.

Laboratory Data.—Blood: Examination of the blood revealed red blood cells, 2.28 million; hemoglobin, 8.3 Gm. (54 per cent); white blood cells, 7,900, and reticulocytes, 1.1 per cent. The mean corpuscular volume was 119 cubic microns, the mean corpuscular hemoglobin was 42 micromicrograms and the mean corpuscular hemoglobin concentration was 32 per cent.

Differential Bone Marrow Counts: In the bone marrow the percentage of cells was as follows: metamyelocytes, 17; myelocytes C, 17; myelocytes B, 3; band neutrocytes, 17; segmented neutrocytes, 26; basophils, none; eosinophils, 3; megakaryocytes, 1; plasma cells, 2; lymphocytes, 13; clasmatocytes, 1, and reticulum cells, none, for a total of 100 per cent. The number of megaloblasts was 4; early erythroblasts, 15; late erythroblasts, 12, and normoblasts, 44.

Gastric Analysis: A fasting specimen of the stomach contents gave a determination of 15 degrees free hydrochloric acid and 20 degrees total acidity. The reading thirty minutes after histamine stimulation was 65 degrees free hydrochloric acid and 75 degrees total acidity.

Serum Protein: The determination of serum proteins was: total, 5.4 Gm., albumin, 3.6 Gm. and globulin, 1.8 Gm., per hundred cubic centimeters. The serum cholesterol reached a total of 225 mg. and the serum cholesterol ester, 180 mg., per hundred cubic centimeters. Other determinations were: cal-

cium, 10.8 mg.; phosphorus, 5.0 mg., and potassium, 13.4 mg., per hundred cubic centimeters. The serum amylase level was 98 units, the serum lipase, 1.3 (cc. of twentieth-normal sodium hydroxide per hundred cubic centimeters).

Stool Analyses: Examination of the stool disclosed that the p_H was 4.5 and the fatty acid, 12.3 cc. of tenth-normal sodium hydroxide (per 100 Gm. of moist feces). Stool examination did not show pathogens or parasites. Specific pathogenic bacteria were not obtained on culture.

Protoscopic Examination: The mucosa was edematous, congested, hypertrophic, slick and of a type compatible with a diagnosis of nutritional deficiency.

Progress.—On admission to the hospital the patient was given the diet previously described. After the completion of base line studies he was given 100 mg. of folic acid twice a day by mouth. On the sixteenth day, the dosage of folic acid was reduced to 100 mg. a day and on the thirty-first day to 25 mg. a day. (This was one of the first cases studied. We have since learned that 10 mg. a day would have produced the same response.) On the fifth day of therapy the reticulocytes began to rise and reached a peak of 12.5 per cent on the eighth day. By the fourteenth day the red blood cells had increased to 2.85 million and the hemoglobin to 10.0 Gm. (65 per cent), a net increase in red blood cells of 0.57 million and in hemoglobin of 1.7 Gm. Thirty days after the initiation of therapy the bone marrow was normoblastic. When the patient was discharged after one hundred and two days on folic acid therapy, examination of the blood showed red blood cells, 4.54 million; hemoglobin, 12.6 Gm. (82 per cent), and reticulocytes, 1.0 per cent. (See figure 6, which shows the hemopoietic response.)

Subjective improvement began on the third day of treatment when the patient volunteered the information that his appetite, strength and vigor had improved. By the sixth day the soreness of his tongue had disappeared, and the redness had begun to fade. By the twentieth day it was normal in appearance, and after forty-three days on therapy the papillae had completely regenerated. During the preliminary period of study he had been having from six to eight foul-smelling, yellow, frothy stools a day with a total volume of from 1,000 to 1,500 cc. They became normal in color, odor and volume, although they were not always completely well formed. Other than slight pitting edema of the ankles, which occurred on the forty-ninth day of treatment and gradually subsided within two weeks, the clinical and hematologic improvement was uninterrupted. When he was discharged after one hundred and two days of therapy he had gained 17 pounds (7.7 Kg.) in weight (fig. 5). He returned to work in a copper mine the day after he was discharged from the hospital. When he returned for follow-up studies two months later, examination of the blood showed red blood cells, 4.80 million; hemoglobin, 12.8 Gm. (83 per cent), and reticulocytes, 0.6 per cent. Bowel movements were occurring only once a day and were normal in color, volume, odor and consistency. He had eaten regularly of the prescribed diet, which included liberal amounts of meat, eggs and milk. Despite having done heavy work in a copper mine eight and one-half hours a day for six days a week from the time he was discharged, he had gained 3 pounds (1.4 Kg.) and had remained asymptomatic.

TABLE 2.—*Antianemic Effect of Folic Acid in Sprue*

Case	Name	Red Blood Cells, Millions			Hemoglobin, Gm.			Reticulocytes, %			Folic Acid Therapy		
											Daily Dosage		Total Days of Administration
		Initial	14th Day	Final Day	Initial	14th Day	Final Day	1st Day of Rise	Day of Peak	% at Peak	Mg.	Days	
1	C. G.	1.47	2.55	3.80	6.8	8.6	11.5	4	6	22.7	200	21	
											100	16	
											25	50	87
2	M. S.	1.99	2.69	3.98	7.2	10.0	12.8	3	6	19.5	200	15	
											100	16	
											25	121	152
3	G. B.	1.53	2.40	4.19	7.1	10.7	11.5	5	8	22.6	10	129	129
4	J. C.	1.57	2.63	4.60	7.0	7.4	13.1	5	8	27.2	10	63	63
5	G. A.	1.28	2.49	4.41	5.9	8.1	14.4	4	6	31.8	200	15	
											100	16	
											25	105	136
6	A. M.	2.13	2.84	4.36	10.1	11.7	13.5	5	8	18.8	10	66	66
7	A. F.	2.16	2.66	4.33	9.5	9.7	13.2	5	7	17.2	200	24	
											100	16	
											25	102	142
8	P. E.	2.28	2.85	4.54	8.3	10.0	12.6	6	8	12.5	200	15	
											100	16	
											25	51	82
9	J. S.	1.97	3.04	4.84	9.7	10.4	15.0	5	7	17.2	200	25	
											100	16	
											25	102	143
10	D. I.	1.32	2.52	3.34	6.5	8.2	14.8	4	6	14.0	10	35	35
11	F. G.	1.63	3.48	4.39	5.9	10.3	12.9	3	6	22.9	200	13	
											100	16	
											25	51	80
12	R. C.	2.61	3.63	4.24	11.0	11.9	13.2	3	8	7.4	5	52	52
13	I. D.	1.95	2.10	4.09	10.2	10.3	12.4	6	12	8.2	10	77	77
14	C. C.	0.98	2.92	4.62	3.8	7.9	15.2	3	7	33.2	10	77	77
15	F. S.	1.64	1.74	3.22	5.2	6.1	6.1	5	9	15.7	10	64	64
16	E. E.	1.25	2.92	3.70	4.6	9.8	11.4	5	9	10.4	10	23	23
17	F. P.	2.52	2.29	2.29	10.7	10.0	9.6	4	10	6.2	10	22	22
18	E. V.	2.60	3.47	4.46	13.2	12.0	13.8	5	8	4.8	10	71	71

COMMENT

Macrocytic anemias occur throughout the world. In the past, many clinicians have considered it essential to divide those cases due to a failure in diet (nutritional macrocytic anemia) from those due to a primary disturbance of the alimentary tract (addisonian pernicious anemia and sprue). Patients with macrocytic anemia with megaloblastic arrest of the bone marrow are studied carefully in our clinic before any attempt at clinical classification is made.[2] Tentatively the diseases of those having achylia after histamine injection are considered as addisonian pernicious anemia. Those having acid steatorrhea are considered as having sprue. The diseases of those having a dietary deficiency without achylia or steatorrhea we call nutritional macrocytic anemia. In an extremely large series of patients one finds persons whose symptoms are difficult to classify in any clearcut clinical syndrome. Indeed, the same patient when seen on different occasions may suggest different syndromes. It is generally considered that there is little essential

2. Moore, C. V.; Vilter, R.; Minnich, V., and Spies, T. D.: Nutritional Macrocytic Anemia in Patients with Pellagra or Deficiency of the Vitamin B Complex, J. Lab. & Clin. Med. **29**: 1226, 1944.

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difference between tropical sprue and nontropical sprue, or celiac disease, and our observations in the United States and in Cuba lend support to this contention. Moore, Bierbaum, Welch and Wright [3] have reported a case of nontropical sprue which responded to folic acid therapy, and Darby, Jones and Johnson [4] reported 3 cases of nontropical sprue which responded similarly.

Folic acid may be expected to exert an effect on macrocytic anemia in relapse in persons whose bone marrow shows megaloblastic arrest, irrespective of the presence or absence of steatorrhea, achylia, pellagra and the like. Unpublished observations by one of us (T. D. S.) show that thiamine, nicotinic acid and riboflavin lack therapeutic value in initiating regeneration of the blood in persons with these characteristic anemias and do not supplement folic acid therapy from the standpoint of regeneration of the blood. In patients with any type of macrocytic anemia a deficiency of these vitamins and iron frequently occurs at the same time, and in persons with sprue or nutritional macrocytic anemia there is also a high incidence of infection and parasitic infestations. These complications make research on the macrocytic anemias a difficult and tedious task. Before the introduction of folic acid there was not a known chemical substance that had any profound effect on the ultimate course of the sprue. The problem is now entirely different, and the present paper shows definitely that this substance is of profound importance in the rehabilitation of patients with sprue.

SUMMARY AND CONCLUSION

The present report shows that persons with sprue can be rehabilitated by the judicious use of synthetic folic acid. After the administration of the folic acid there was a prompt regeneration of the blood and a tendency of the alimentary tract to return to normal function. Despite the fact that antiparasitic therapy was not administered, the presence of pathogenic intestinal parasites did not prevent these persons from being profoundly benefited. (We make no claim that the folic acid in any way adversely affected the parasites, and all our examinations indicated that they continued to thrive in the intestinal tracts of our patients.) We do not recommend, in the day to day practice of medicine, that persons with sprue be given a deficient diet such as the one used in this study. In fact, we stress the desirability of prescribing a diet adequate in protein, vitamins and minerals. Of 18 patients rehabilitated, 5 are women who have returned to their full household duties. Nine of the 13 men have returned to work, 9 to their former jobs and 1 to a better job than he had prior to his illness. One of the 4 men (case 9) not working is a cripple who has never been able to work. The other 3, who are 75 years of age (cases 7, 15 and 16), had retired. These 4 patients, however, are able to care for themselves, whereas prior to treatment they had been bedridden and dependent on their families or friends for their personal care. Case 6 is representative of a man who returned to his former job as a wood-cutter. Case 8 is described in detail as an example of a man who returned to industrial work. Examination two months later has revealed that both are in excellent health. Neither one of them has missed a day's work since being discharged from the hospital.

3. Moore, C. V.; Bierbaum, O. S.; Welch, A. D., and Wright, L. D.: The Activity of Synthetic Lactobacillus Casei Factor ("Folic Acid") as an Antipernicious Anemia Substance: Observations on Four Cases; Two with Addisonian Pernicious Anemia, One with Non-Tropical Sprue and One with Pernicious Anemia of Pregnancy, J. Lab. & Clin. Med. **30:** 1056, 1945.

4. Darby, W. J.; Jones, E., and Johnson, H. C.: Effect of Synthetic Lactobacillus Casei Factor in Treatment of Sprue, J. A. M. A. **130:** 780 (March 23) 1946.

PARA-AMINOBENZOIC ACID TREATMENT OF ROCKY MOUNTAIN SPOTTED FEVER

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The use of *p*-aminobenzoic acid (PABA) in the treatment of several of the rickettsial diseases has been reported recently. Following the experimental work of various investigators, Yeomans, Snyder, Murray, Zarafonetis and Ecke [1] gave the clinical results of the effect of *p*-aminobenzoic acid given orally to 20 patients with louse-borne typhus in Egypt. The course of the disease was favorably modified when treatment was begun early. Tierney [2] in an exceedingly well controlled study showed conclusively that the drug is effective therapeutically in tsutsugamushi fever or scrub typhus. He reported the cases of 34 patients with this disease between the ages of 21 and 45, 18 of whom received *p*-aminobenzoic acid. None of the treated patients died, whereas 3 of the 16 untreated succumbed. More convincing was the prompt drop in temperature and the subsidence of symptoms following the administration of *p*-aminobenzoic acid to the patients who recovered. A large dosage of the drug was given, and high levels were obtained in the blood. Minor toxic effects were observed in the patients receiving exceedingly high dosage. The optimum blood level was finally considered to be 30 to 60 mg. per hundred cubic centimeters.

Previously, experimental work by Anigstein and Bader [3] and by Hamilton, Plotz and Smadel [4] indicated that spotted fever rickettsias were even more susceptible to *p*-aminobenzoic acid than the typhus rickettsias. The first report of a case of spotted fever treated with this drug was by Rose, Duane and Fischel.[5] The patient contracted the disease on Long Island, N. Y., and the administration of *p*-aminobenzoic acid apparently exercised a beneficial effect. Maroney, Davis and Scott [6] reported a similar result in the first case of spotted fever so treated in Delaware. We are now reporting additional cases.

PREVIOUS STATUS OF DISEASE IN DELAWARE

In properly evaluating any new mode of therapy in a disease such as Rocky Mountain spotted fever, the preexisting status of the disease in the particular area concerned is most important. Dyer [7] in 1934 estimated

This study was made through the cooperation of the Delaware, Memorial, St. Francis and Wilmington General Hospitals and through the courtesy of the following physicians in submitting the case records of their patients for analysis: Charles M. Bancroft, Ira Burns, Harry A. Carl, I. Lewis Chipman, G. W. K. Forrest, Walter S. Lumley, John Maroney, Arthur A. Mencher, Edgar R. Miller, E. Hughes Nutter, Edward Parvis, D. Duer Reynolds, Everett Reynolds, John E. Robbins, William Silverman, M. F. Squires Jr., Roger Thomas, J. William Urie and Norwood W. Voss.

1. Yeomans, A.; Snyder, J. C.; Murray, E. S.; Zarafonetis, C. D. J., and Ecke, R. S.: The Therapeutic Effect of Para-Aminobenzoic Acid in Louse Borne Typhus Fever, J. A. M. A. **126:** 349-356 (Oct. 7) 1944; correction, ibid. **126:** 581 (Oct. 28); 782 (Nov. 18) 1944.

2. Tierney, N. A.: Para-Aminobenzoic Acid in Tsutsugamushi Disease, J. A. M. A. **131:** 280-285 (May 25) 1946.

3. Anigstein, L., and Bader, M. N.: Para-Aminobenzoic Acid: Its Effectiveness in Spotted Fever in Guinea Pigs, Science **101:** 591-592, 1945.

4. Hamilton, H. L.; Plotz, H., and Smadel, J. E.: Effect of Para-Aminobenzoic Acid on the Growth of Typhus Rickettsiae in the Yolk Sac of the Infected Chick Embryo, Proc. Soc. Exper. Biol. & Med. **58:** 255-262, 1945.

5. Rose, H. M.; Duane, R. B., and Fischel, E. E.: The Treatment of Spotted Fever with Para-Aminobenzoic Acid, J. A. M. A. **129:** 1160-1161 (Dec. 22) 1945.

6. Maroney, J. W.; Davis, H. C., and Scott, E. G.: Rocky Mountain Spotted Fever: A Case Treated with Para-Aminobenzoic Acid, Delaware State M. J. **18:** 104-106, 1946.

7. Dyer, R. E.: Rocky Mountain Spotted Fever, Delaware State M. J. **6:** 52-55, 1934.

the mortality of the eastern type of Rocky Mountain spotted fever as 25 per cent; later the same author [8] gave the crude mortality for the disease for the entire country as 18 per cent. The Delaware State Board of Health [9] reports that in the ten year period from 1936 to 1945, inclusive, 50 cases were reported in Delaware. Of those 50 cases, 14 were fatal, a mortality of 28 per cent. A well defined difference in the fatality rate occurred in patients over the age of 40. There were 23 patients over the age of 40, of whom 12 died, a mortality rate of 52 per cent. There were 27 under the age of 40, with 2 deaths, or a mortality rate of about 7 per cent. We have analyzed the records of 31 cases (table 1) of Rocky Mountain spotted fever occurring in the Wilmington, Del., area from 1938 to 1946, inclusive. Twenty-one patients were not treated with *p*-aminobenzoic acid. The fatality rate is similar to that given previously for the entire state (table 2). Of the 21 patients, 5 died, or 24 per cent. There were 6 patients over the age of 40 (group *A*, table 1), of whom 3 died, or 50 per cent. Of the 15 patients under 40 years of age, (group *B* and *C*, table 1), 2 died, or a mortality of 13 per cent. It is evident, therefore, that in this particular area Rocky Mountain spotted fever is of a fairly severe type.

TABLE 1.—*Summary of Thirty-One Cases of Rocky Mountain Spotted Fever in Delaware*

	Case	Age	Sex	Year	Day of Disease Admitted to Hospital	Days of Continuous Fever	Rash, Day of Disease	Day of Disease PABA Started	Total PABA Dosage, Gm.	Maximum PABA Blood Level, Mg./100 Cc.	Days of Fever After PABA Started	Proteus OX 19 Changing Titer	Result
Group A. Patients over 40 yrs. of age not treated with PABA	1	48	♂	1938	..	15	3	..	.....	....	..	Negative-1:1,280	Died
	2	51	♀	1941	7	15	4	..	.....	....	..	Negative-1:100	Recovered
	3	60	♂	1941	15	39	13	..	.....	....	..	Negative-1:3,250	Recovered
	4	73	♀	1941	5	24	8	..	.....	....	..	Negative-1:80	Recovered
	5	52	♂	1944	3	10	3	..	.....	....	..	Negative-1:320	Died
	6	63	♂	1946	5	5	4	..	.....	....	..	1:40	Died
Group B. Fatal cases, patients under 40 yrs. of age not treated with PABA	7	33	♂	1944	6	12	6	..	.....	....	..	1:80	Died
	8	3	♂	1945	4	10	3	..	.....	....	..	Negative	Died
Group C. 13 patients under 40 yrs. of age recovering without PABA	9	23	♀	1941	13	20	8	..	.....	....	..	Negative-1:460	Recovered
	10	7	♀	1941	6	16	4	..	.....	....	..	Negative-1:400	Recovered
	11	22	♀	1941	10	11	8	..	.....	....	..	Negative-1:320	Recovered
	12	7	♀	1942	6	14	4	..	.....	....	..	Negative, not tested 2d wk.	Recovered
	13	14	♂	1942	5	20	5	..	.....	....	..	Negative-1:320	Recovered
	14	10	♂	1943	6	13	4	..	.....	....	..	Negative-1:160	Recovered
	15	11	♀	1943	8	11	?	..	.....	....	..	1:320 -1:1,280	Recovered
	16	3	♂	1943	7	29	9	..	.....	....	..	Negative-1:320	Recovered
	17	9	♀	1943	7	17	6	..	.....	....	..	Strongly pos.	Recovered
	18	7	♂	1944	10	23	10	..	.....	....	..	Negative, not tested 2d wk.	Recovered
	19	7	♀	1944	3	17	2	..	.....	....	..	Negative, not tested 2d wk.	Recovered
	20	4	♀	1945	5	13	3	..	.....	....	..	Negative-1:320	Recovered
	21	23	♂	1946	9	19	7	..	.....	....	..	1:160 -1:20,000	Recovered
Group D. 9 patients under 40 yrs. of age recovering with PABA	22	3	♀	1946	9	15	4	13	60.8	29.0	4	1:40 -1:640	Recovered
	23	8	♂	1946	6	10	3	7	50.4	18.5	2	1:20 -1:640	Recovered
	24	11	♀	1946	5	13	3	8	67.0	6.5	3	Negative-1:320	Recovered
	25	11	♀	1946	6	12	4	7	145.0	23.5	5	Negative-1:640	Recovered
	26	22	♀	1946	5	7	3	6	114.0	22.1	1	1:80 -Neg.	Recovered
	27	32	♀	1946	3	8	3	4	162.0	26.0	2	Negative-1:320	Recovered
	28	37	♀	1946	3	7	4	3	270.6	Not done	3	Not tested	Recovered
	29	12	♂	1946	8	14	7	9	162.0	48.0	3	Negative-1:20,480	Recovered
	30	36	♂	1946	6	12	4	6	327.0	39.0	5	1:80 -1:1,600	Recovered
Group E. patient over 40 yrs. of age treated with PABA	31	67	♂	1946	8	16	4	8	211.0	80.0	9	1:160 -1:80	Died *

* At autopsy, small granular kidneys indicating severe long-standing renal disease were found.

TREATMENT WITH PARA-AMINOBENZOIC ACID

In this series of 10 patients treated with *p*-aminobenzoic acid, 9 under the age of 40 responded dramatically (group *D*, table 1). The records of these patients are very striking when compared to those of 13 patients (group *C*, table 1) under the age of 40 who recovered without receiving *p*-aminobenzoic acid (table 3). The average number of days of fever in the untreated patients was 17.5, as compared to 10.5 for the patients given *p*-aminobenzoic acid. The untreated patients averaged twenty hospital days; those treated, thirteen days. In the treated patients there was a decided clinical improvement twenty-four hours before the temperature started to drop. The temperature of patients given *p*-aminobenzoic acid dropped rapidly to normal within two to four days after treatment was begun, whereas in the untreated patients the temperature gradually came down to normal over a period of about sixteen hospital days. Coincidental with the lowering of the temperature the rash rapidly faded, and the patient made a prompt clinical recovery. The average day of disease on admission to the hospital was 7.2 days for the untreated patients and 5.5 days for those given *p*-aminobenzoic acid. The average day of disease on which therapy was begun was 7.6 days or about the same day of disease as that on which the untreated patients were admitted to the hospital. Composite curves of the maximum average daily temperature (chart 1) in the two groups is especially striking.

CLINICAL EXPERIMENTAL STUDIES WITH PARA-AMINOBENZOIC ACID

Para-aminobenzoic acid is known to be rapidly excreted by the body [10] and consequently the maintenance of a steady effective level in the blood necessitates frequent administration of the drug. In order to select

8. Dyer, R. E.: The Rickettsial Diseases, J. A. M. A. **124:** 1165-1172 (April 22) 1944.

9. Delaware State Board of Health: Personal communication to the authors.

10. (*a*) Zehender, F.: Ueber die Acetylierung von primären Aromatischen Aminen in Vivo und in Vitro, Helvet. chim. acta **26:** 1339, 1943. (*b*) Kirch, E. R., and Bergeim, O. J.: Determination of Para-Aminobenzoic Acid, J. Biol. Chem. **148:** 445, 1943.

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1946

the most favorable mode and schedule of therapy, studies were made of the blood levels and urinary excretion rates following administration of the drug in three different ways: (1) orally in aqueous sodium bicarbonate, (2) as 0.5 Gm. tablets of the sodium salt and (3) intravenously as the sodium salt.[11] The drug concentrations were determined by Bratton and Marshall's [12] sulfonamide procedure as modified by Eckert.[13] Although this method permits differentiation between free and coupled *p*-aminobenzoic acid as far as the amino group is concerned, it does not yield information on the extent of coupling on the carboxyl group to yield such products as *p*-aminohippuric acid, which according to Smith [14] occurs extensively.

These studies have shown, in agreement with those of Zehender [10a] and Kirch and Bergeim,[10b] that within four hours following the administration of *p*-aminobenzoic acid by any of the three methods already mentioned essentially all of the drug has disappeared from the blood stream. During this time 70 to 80 per cent may be recovered in the urine; about 25 per cent of the material excreted is coupled on the amino group. In chart 2 the average blood levels obtained in two series of eight experiments are plotted as a function of time. One series of patients received 3 Gm. of *p*-aminobenzoic acid in a solution of sodium bicarbonate, the other 3 Gm. of the sodium salt of *p*-aminobenzoic acid as six 0.5 Gm. tablets. These results suggest that, due to its slower absorption, more prolonged and steadier levels of the drug in the blood may be obtained with the tablet form and emphasize the importance of administration of the drug at least every two hours and perhaps more frequently if the bicarbonate solution is used. Considerable variations in the maximum blood levels following the oral administration of *p*-aminobenzoic acid, in bicarbonate solution and as the sodium salt in tablet form, were obtained. These variations probably result from individual differences in the subjects studied and may be related to the fluid balance (group *D*, table 1).

TABLE 2.—*Rocky Mountain Spotted Fever in Delaware, Para-Aminobenzoic Acid Not Given*

	50 Cases (1936-1945)		21 Cases (1938-1946)		
Number of Cases	Number Died	Per Cent Died	No. of Cases	Number Died	Per Cent Died
Total (50)	14	28	21	5	24
23 over 40 yrs.	12	52	6	3	50
27 under 40 yrs.	2	7	15	2	13

TABLE 3.—*Comparison of Cases With and Without Para-Aminobenzoic Acid Therapy*

	Average Day of Disease Admitted to Hospital	Average Days of Continuous Fever	Average Day of Disease PABA Began	Average Days of Fever After PABA	Average Days of Fever After 7th Day
9 patients under 40 yrs. with PABA.....	5.5	10.5	7.6	3	3.0
13 patients under 40 yrs. without PABA.....	7.2	17.5	...	..	10.3

Parenteral administration of *p*-aminobenzoic acid may be desirable in the occasional patient who cannot retain the material by mouth or in the comatose patient who cannot swallow. As seen in chart 2, *p*-aminobenzoic acid is excreted rapidly when given intravenously. In the few instances when it must be given parenterally

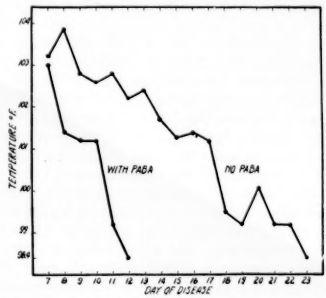

Chart 1.—Comparison of average highest daily temperatures in 9 cases of Rocky Mountain spotted fever treated with *p*-aminobenzoic acid, and in 13 cases not so treated.

continuous intramuscular drip, as suggested by Woodward,[15] is probably the preferable method. A 25 per cent solution of sodium *p*-aminobenzoic acid in isotonic solution of sodium chloride is used. This solution is sterilized by filtration by a Seitz filter bringing the p_H to approximately 7.0 by the addition of small amounts of crystalline *p*-aminobenzoic acid to the solution of sodium *p*-aminobenzoic acid before filtration.

DIAGNOSIS

The great majority of the cases reported had all the criteria for diagnosis—tick bite, fever, typical rash and a changing agglutination titer for Proteus OX19. In a few cases the agglutination titer was not determined in the second week of the disease. In every such instance, however, the patient contracted the disease during the tick season in a locality known to be infected, and the

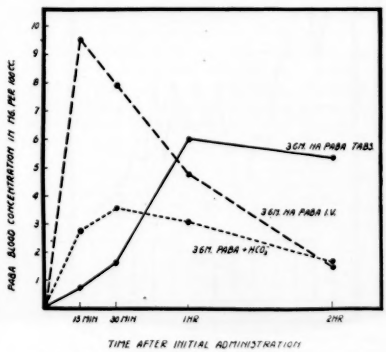

Chart 2.—Result of eight clinical experiments in normal persons to determine blood levels when *p*-aminobenzoic acid was given by mouth in 5 per cent sodium bicarbonate solution, when sodium *p*-aminobenzoic acid tablets were given and when the sodium salt was given intravenously.

11. The Para-Aminobenzoic Acid used in this work was furnished by Merck & Co., Inc., Rahway, N. J. Tablets and Sterile Intravenous Sodium PABA were furnished by the International Vitamin Corporation, 22 East Fortieth Street, New York 19.

12. Bratton, A. C., and Marshall, E. K., Jr.: A New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128:** 537, 1939.

13. Eckert, H. W.: Determination of Para-Aminobenzoic Acid, Conjugated Para-Aminobenzoic Acid, and Para-Nitrobenzoic Acid in Blood, J. Biol. Chem. **148:** 197, 1943.

14. Smith, P. K.: The Use of Para-Aminobenzoic Acid in Endemic (Murine) Typhus, J. A. M. A. **131:** 1114-1117 (Aug. 3) 1946.

15. Woodward, T. E.: Personal communication to the authors.

rash was characteristic, occurring first on the wrists and ankles, then on the palms and soles and later spreading to the trunk. We consider that the diagnosis was correct in each case.

ILLUSTRATIVE CASES

Certain details of the records of 3 of the treated patients will serve to illustrate important points in the clinical use of *p*-aminobenzoic acid. Case 28 (chart 3) shows a secondary rise of temperature presumably due to a too rapid reduction in the dosage of *p*-aminobenzoic acid after the initial clinical response of the patient. Not only was the dosage decreased, but the interval of the doses was increased from two to three hours. Tierney [2] reported similar occurrences in scrub typhus when the dosage was reduced too soon. In this instance agglutination and blood level studies were not performed. The diagnosis, although not definitely proved, is almost certainly correct. A swollen tick was removed from the patient three days before she became suddenly ill with fever, headache and prostration, and on the fourth day a typical rash appeared.

Cases 29 and 30 are of interest in illustrating the importance of the control of fluid balance, especially the urinary output, in maintaining the *p*-aminobenzoic acid level in the therapeutic range. In case 29 (chart 4) when the twenty-four-hour urinary output was between 250 and 500 cc., the *p*-aminobenzoic acid blood level was 46 and 48 mg. per hundred cubic centimeters on a daily dosage of about 12 Gm. Later, when the output was 1,500 to 1,600 cc., the blood level dropped to 10 and 4 mg. with a higher daily dosage of 20 Gm.

Again in case 30 (chart 5) with daily doses of 36 to 54 Gm. of *p*-aminobenzoic acid, the blood level ranged only from 7 to 12 to 5 mg. until the urinary output was reduced from 1,300 cc. to 500 cc. The level then promptly jumped to 39 mg.; and the temperature, which

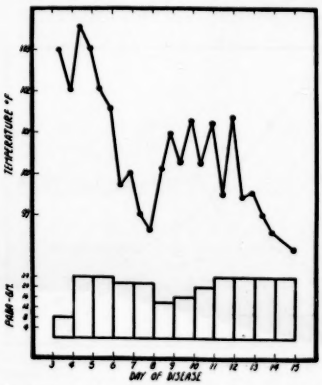

Chart 3 (case 28).—Secondary rise of temperature when dosage of *p*-aminobenzoic acid was reduced too soon.

had been falling slowly, dropped abruptly. Smith [14] reported the use of *p*-aminobenzoic acid in 29 cases of endemic (murine) typhus. The results were certainly beneficial but not so striking as in Tierney's [2] cases of scrub typhus or in the cases of Rocky Mountain spotted fever here reported. Smith gave 2 Gm. of the drug every two hours routinely without measuring blood levels routinely. If blood levels were estimated daily at the same time interval, preferably two hours, after the preceding oral dose of the medicament and if more attention were given to the urinary output in order to maintain a blood level between 30 and 60 mg. per hundred cubic centimeters, perhaps a clinical response

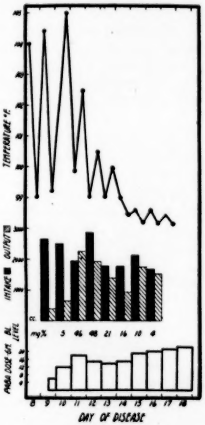

Chart 4 (case 29).—Showing a high blood level with a small dose of *p*-aminobenzoic acid and low urinary output and a low blood level with a higher dosage of *p*-aminobenzoic acid when the urinary output was increased.

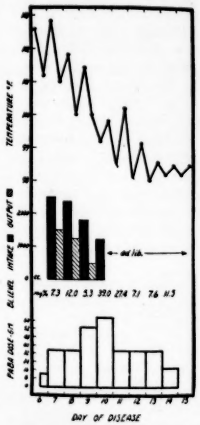

Chart 5 (case 30).—Showing difficulty in securing adequate blood level of *p*-aminobenzoic acid until the urinary output was reduced.

might be obtained in patients with endemic typhus comparable with that obtained in those with scrub typhus and Rocky Mountain spotted fever.

The 1 fatality in our series was the only patient over the age of 40. He was aged 67 and refused admission until the eighth day of the disease, the fourth day of the rash. At this time he was mentally confused and had a blood urea nitrogen level of 60 mg. per hundred cubic centimeters. In spite of this he was able to swallow the *p*-aminobenzoic acid and absorbed enough to maintain a blood level of 48 to 80 mg. per hundred cubic centimeters for five days, when he died in uremia. At autopsy the kidneys were found to be small, granular and typical of long-standing renal disease. Evidently, therefore, he had had renal damage antedating the onset of his Rocky Mountain spotted fever. He also had had a previous myocardial infarction. This case may serve to illustrate the point that experimental work [16] has suggested—namely, that *p*-aminobenzoic acid retards or prevents the spread and proliferation of the rickettsias in the body but is not an antidote for any toxin already released and does not repair damage already done. Therefore the beneficial effect of the medicament in late cases is unlikely.

SUMMARY

1. Ten cases of Rocky Mountain spotted fever treated with *p*-aminobenzoic acid are reported and are compared with 21 control cases of Rocky Mountain spotted fever not treated with *p*-aminobenzoic acid.

16. Greiff, D.; Pinkerton, H., and Moragues, V.: Effect of Enzyme Inhibitors and Activators on the Multiplication of Typhus Rickettsiae: Penicillin, Para-Aminobenzoic Acid, Sodium Fluoride and Vitamins in B Group, J. Exper. Med. **80**:561-574, 1944. Hamilton, Plots and Smadel.[4]

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2. All 9 treated patients under 40 years of age recovered. One patient over 40 years of age with complications due to cardiorenal disease died.

3. In 21 untreated patients there were five deaths—2 in patients under 40, 3 in patients over 40 years of age.

4. The length of fever in untreated patients was 17.5 days as compared to 10.5 days for those given *p*-aminobenzoic acid.

5. Most of the treated patients showed dramatic clinical improvement shortly after treatment began.

6. The *p*-aminobenzoic acid was administered without complication.

7. Because of the rapid urinary excretion of the compound, oral administration at one or two hour intervals is required to maintain therapeutic blood levels.

8. Individual variation in blood levels requires the adjustment of dosage and fluid balance.

9. The tablet form of sodium *p*-aminobenzoic acid produced more prolonged and steadier levels of the drug in the blood in clinical experiments on 8 volunteers.

CONCLUSION

Para-aminobenzoic acid was found to be most effective in the treatment of 10 cases of Rocky Mountain spotted fever in Delaware.

Clinical studies suggest that the level of *p*-aminobenzoic acid in the blood is best kept in the optimum range of 30 to 60 mg. per hundred cubic centimeters by adjustment of dosage and fluid balance in each individual case.

TOXIC REACTIONS ACCOMPANYING PENICILLIN THERAPY

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Since Fleming's [1] observations on the antibacterial action of penicillium in 1929, toxic reactions produced by and accompanying the clinical use of this medicament have constituted an important part of the extensive literature on penicillin. The observations by my associates and me are incorporated in the various papers [2] from Bushnell General Hospital; the papers by Lyons,[2b] Keyes [2c] and Morginson [2i] particularly discuss toxic reactions. The findings made at Bushnell General Hospital agree with those of other authors and will not be listed separately.

In the short time at my disposal, it will be impossible to discuss in detail all the reactions that have been enumerated as following penicillin therapy. These are listed in the various tables. This paper will present salient observations concerning each group of symptoms. The adverse symptoms produced by penicillin may be grouped and will be discussed according to its role as (1) direct toxin and primary irritant, (2) antigen, (3) therapeutic shock excitant and (4) indirect action on pathologic processes.

DIRECT TOXIN AND PRIMARY IRRITANT

Crude and commercial penicillin is not a direct toxin in concentrations permitting its therapeutic use. Fleming [1] was the first to show that subcutaneous and intraperitoneal injections and irrigations of large surfaces and of the conjunctivas had no ill effects. Subcutaneous injections in mice, rats and cats produced no sloughs, and blood concentrations to 5,000 units per cubic centimeter had no deleterious effects.[3] In mice, the toxic dose is about sixty-four times the effective dose as determined by subcutaneous injections of crude penicillin.[4] A wide variance in lethal doses for mice, ranging from 3,500 to 32,000 units, was observed when three hundred lots from fourteen manufacturers were tested.[5]

Human leukocytes remain active in 1,000 units per cubic centimeter for at least three hours.[6] Daily doses of 400,000 units in experimental animals produced no injury to kidneys, liver, bone marrow or brain [7] and low toxicity for tissue cells as measured by means of in vitro methods of tissue culture.[8] Apparently there is no disturbance of the peripheral blood or hemopoietic system, and penicillin can be used in the presence of pronounced anemia, leukopenia and agranulocytosis.[7b]

It has not been determined whether the minimal direct toxic action of penicillin depends on impurities contained in the corn mash or steep, chemicals used to remove pyrogens or other products in commercial penicillin, as little comparative work has been done on the toxicology of crystalline penicillin. Purification, apparently, reduces toxicity.[3b] The toxic action does in part depend on the cation radical, as intravenous toxicity in mice increased progressively with the use of the sodium, ammonium, strontium, calcium, magnesium and potassium salts.[9] Gottschalk and Weiss [10] stated that commercial penicillin is not a primary cutaneous irritant.

For practical purposes the possibilities of penicillin as a direct toxic agent are negligible [11] except, as will be noted, following its intrathecal use.

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1. Fleming, A.: On the Antibacterial Action of Cultures of a Penicillin, with Special Reference to Their Use in the Isolation of B. Influenzae, Brit. J. Exper. Path. **10:** 226 (June) 1929.

2. Papers from Bushnell General Hospital: (*a*) Hollenberg, H. G.: Letter, J. Arkansas M. Soc. **40:** 134 (Dec.) 1943. (*b*) Lyons, C.: Penicillin Therapy of Surgical Infections in the U. S. Army, J. A. M. A. **123:** 1007 (Dec. 18) 1943. (*c*) Keyes, J. E. L.: Recent Advances in Ophthalmology, Ohio State M. J. **39:** 1110 (Dec.) 1943; (*d*) Penicillin in Ophthalmology, J. A. M. A. **126:** 610 (Nov. 4) 1944. (*e*) Putney, F. J.: Uses of Penicillin in Diseases of Nose and Throat, ibid. **126:** 620 (Nov. 4) 1944. (*f*) Bosworth, N. L.; Riba, L. W., and Schmidlapp, C.: Two Hundred and Thirty-Three Cases of Sulfa-Resistant Gonorrhea Treated with 50,000 Units of Penicillin, J. Urol. **52:** 631 (Dec.) 1944. (*g*) Sweeney, J. S.; Morginson, W. J.; Robinson, R. W., and Kilpatrick, E. M.: Therapeutic Effectiveness of Penicillin in Treatment of Vincent's Stomatitis and Its Failure to Influence Favorably Certain Other Medical Conditions, J. Lab. & Clin. Med. **30:** 132 (Feb.) 1945. (*h*) Putney, F. J.: Penicillin in Mastoiditis and Its Complications, Arch. Otolaryng. **41:** 247 (April) 1945; (*i*) Morginson, W. J.: The Clinical Use of Penicillin in Dermatology, South. M. J. **38:** 320 (May) 1945. (*j*) Naegeli, F. C., and Morginson, W. J.: Treatment of Vincent's Infection with Penicillin, J. Am. Dent. A. **32:** 1393 (Nov. 1-Dec. 1) 1945.

3. (*a*) Chain, E.; Florey, N. W.; Gardner, A. D.; Jennings, M. A.; Orr-Ewing, J., and Sanders, A. G.: Penicillin as a Chemotherapeutic Agent, Lancet **2:** 226 (Aug. 24) 1940. (*b*) Hamre, D. M.; Rake, G.; McKee, C. M., and MacPhillamy, H. B.: Toxicity of Penicillin as Prepared for Clinical Use, Am. J. M. Sc. **206:** 642 (Nov.) 1943. (*c*) Hobby, G. L.; Meyer, K., and Chaffee, E.: Chemotherapeutic Activity of Penicillin, Proc. Soc. Exper. Biol. & Med. **50:** 285 (June) 1942.

4. Robinson, H. J.: Toxicity and Efficacy of Penicillin, J. Pharmacol. & Exper. Therap. **77:** 70 (Jan.) 1943.

5. Welch, H.; Price, C. W.; Nielson, J. K., and Hunter, H. G.: The Acute Toxicity of Commercial Penicillin, J. Lab. & Clin. Med. **29:** 809 (Aug.) 1944.

6. (*a*) Abraham, E. P.; Chain, E.; Fletcher, C. M., and Florey, H. W.: Further Observations on Penicillin, Lancet **2:** 177 (Aug. 16) 1941. (*b*) Chain and Colleagues.[3a]

7. (*a*) Bloomfield, A. L.; Rantz, L. A., and Kirby, W. M. M.: The Clinical Use of Penicillin, J. A. M. A. **124:** 627 (March 4) 1944. (*b*) Herrell, W. E.; Nichols, D. R., and Heilman, D. H.: Penicillin: Its Usefulness, Limitations, Diffusion and Detection, with Analysis of One Hundred and Fifty Cases in Which It Was Employed, J. A. M. A. **125:** 1003 (Aug. 12) 1944.

8. Herrell, W. E., and Heilman, D. H.: Tissue Culture Studies on Cytotoxicity of Bactericidal Agents, Am. J. M. Sc. **205:** 157 (Feb.) 1943; **206:** 221 (Aug.) 1943. Footnotes 6 and 7*b*.

9. Welch, H.; Grove, D. C.; Davis, R. P., and Hunter, A. C.: The Relative Toxicity of Six Salts of Penicillin, Proc. Soc. Exper. Biol. & Med. **55:** 246 (April) 1944. Welch and associates.[5]

10. (*a*) Gottschalk, H. R., and Weiss, R. S.: Epidermal Sensitivity to Penicillin, Arch. Dermat. & Syph. **53:** 365 (April) 1946; (*b*) Penicillin Ointment in the Treatment of Some Infections of the Skin, ibid. **53:** 226 (March) 1946.

11. Dawson, M. H., and Hobby, G. L.: The Clinical Use of Penicillin, J. A. M. A. **124:** 611 (March 4) 1944.

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ANTIGEN

Experimental evidence and clinical observation indicate that commercial penicillin and crystalline penicillin possess definite antigenic and allergenic properties.[12] These may be excited by impurities encountered in commercial penicillin, pyrogens, chemicals used to remove pyrogens and crystalline penicillin.[13] It is generally conceded that antigenic reactions are becoming less frequent as impurities are removed from commercial penicillin; the early, dark-colored products seemed to produce more frequent and violent reactions than the later, clearer solutions.[14] Cormia and colleagues, however, stated that no correlation could be observed between the color of commercial penicillin and toxicity.[15] Many of the impurities can be removed by Seitz filtration.[16] Reactions are probably due to impurities when different lots and products of different manufacturers fail to repeat symptoms or give negative reactions to sensitivity tests.[15a]

TABLE 1.—*Reactions Produced by Antigen Properties of Penicillin*

1. Erythema: blotchy, diffuse, morbilliform, scarlatiniform, flushing of face, dermatitis medicamentosa, exfoliating dermatitis	2. Urticaria: sparse, mild, diffuse, massive, transient, acute, chronic, pruritic
3. Angioneurotic edema: localized, lips, eyes, tongue, uvula, pharynx, epiglottis, larynx, diffuse, solid	4. Erythema multiforme, erythema nodosum, edema of joints, polyarthritis, painful adenopathy, myalgia
5. Malaise, headaches, generalized aching, chills, fever, nausea and vomiting, abdominal cramps	6. Dyspnea, pulmonary edema, acute syncope, shock
7. Dizziness, vertigo, muscular twitching, convulsions, loss of consciousness	8. Euphoria and laughing, psychotic depression, agitation, confusion, nervousness
9. Epistaxis, petechiae, purpura, regional anglitis	10. Eosinophilia, pseudoalbuminuria, hematuria, azotemia
11. Tingling in testes, epididymitis	12. Thrombophlebitis
13. Exacerbation latent trichophytosis, trichophytids, dyshidrosis	14. Photosensitization
15. Drug and serum sickness-like syndrome	16. Precipitated latent epilepsy

Sensitization attributes of commercial penicillin have been demonstrated by positive intradermal reactions,[17] by indirect or passive transfer tests of Prausnitz-Kustner,[18] by precipitin reactions [13a] and, in guinea pigs, by Schultz-Dale tests.[19] Positive intradermal reactions,[20] Prausnitz-Kustner reactions [13d] and positive Arthus phenomena [13b] are observed with crystalline penicillin. Heterophil agglutinins have been reported increased by Lyons [2b] and not increased by Cormia.[13a] The latter author also stated that precipitin and passive transfer tests furnish variable results and that conclusive evidence of circulatory antibodies has not been demonstrated. Patch tests have elicited positive reactions to commercial penicillin [21] and to crystalline penicillin.[21a]

Sensitivity to penicillin may be manifested as immediate reactions and delayed reactions.[15a] The immediate reactions usually occur in persons with a known history of penicillin sensitivity or at least previous exposure to penicillin, although a small percentage of the population is primarily or spontaneously sensitive to penicillin.[22] It is doubtful if natural, inherited sensitivity, without previous exposure, exists, because contact may have been intrauterine or the patient may possess a general sensitivity to molds.[23] Herrell, Nichols and Heilman [7b] and others [24] have demonstrated the transmission of penicillin through the placenta from the maternal to the fetal circulation. Jadassohn, Schaaf and Wohler,[25] working with trichophytins, by the Schultz-Dale technic, concluded that fungi have a common antigenic factor in addition to antigenic factors peculiar to each species. Persons may be sensitive to penicillin because they possess a common sensitivity to all molds. Cormia [15a] and Lamb [18a] stated the belief that an exacerbation of a previous fungous infection or vesicular eruptions involving the feet, hands and groins following penicillin therapy may represent this common antigenic factor to molds.

Delayed or acquired sensitivity may be produced by repeated intradermal injections of penicillin [20] or by repeated local applications [10a] and is analogous to drug or serum sensitivity.[26] Sensitivity to penicillin may be of short duration or it may last for considerable periods, even months, and it is conceivable that it may be permanent.[13a] Toxic symptoms may not be noticed until several weeks following continuous injections.[13d] The antigenic potentialities may be latent, requiring lowering of allergic resistance and augmentation with other antigens to present symptoms.[27]

Penicillin sensitivity may be epidermal [28] or dermal,[15a] although the principal shock tissue seems to be the

12. Vermilye, H. N.: Aerosol Penicillin in General Practice, J. A. M. A. **129:** 250 (Sept. 22) 1945. Lyons.[2b]

13. (*a*) Crieg, L. H.: Allergy to Penicillin, J. A. M. A. **126:** 429 (Oct. 14) 1944. (*b*) McClosky, W. T., and Smith, M. I.: Experiments on the Sensitizing Properties of Penicillin, Proc. Soc. Exper. Biol. & Med. **57:** 270 (Nov.) 1944. (*c*) Price, I. C.: Severe Allergic Reaction to Intramuscular Penicillin, Canad. M. A. J. **53:** 485 (Nov.) 1945. (*d*) Kolodny, M. H., and Denhoff, E.: Reactions in Penicillin Therapy, J. A. M. A. **130:** 1058 (April 20) 1946. (*e*) Lyons.[2b] (*f*) Abraham and associates.[6b]

14. Craig, W. M.; Thompson, G. J.; Hutter, A. M.; Barksdale, E. E.; Pfeiffer, C. C., and Wooley, P. V., Jr.: Penicillin: A Progress Report, U. S. Nav. M. Bull. **44:** 453 (March) 1945. Rake, G.; McKee, E. M.; Hanire, D. M., and Houck, C. L., Jr.: Studies on Penicillin: II. Observations on Therapeutic Activity and Toxicity, J. Immunol. **48:** 217 (May) 1944. Penicillin Purified, Editorial, Lancet **2:** 198 (Aug. 15) 1942. Florey, H. W., and Jennings, M. A.: Some Biological Properties of Highly Purified Penicillin, Brit. J. Exper. Path. **23:** 210 (June) 1942. Lyons.[2b] Robitson.[4] Bloomfield and associates.[7a]

15. (*a*) Cormia, F. E.; Jacobsen, L. Y., and Smith, E. L.: Reactions to Penicillin, Bull. U. S. Army M. Dept. **4:** 694 (Dec.) 1945. (*b*) Finebury, S. M.: Penicillin Allergy, J. Allergy **15:** 271 (July) 1944.

16. McClosky and Smith.[5b] Lyons.[2b]

17. Feinberg, S. M.: Penicillin Allergy: On the Probability of Allergic Reactions in Fungus-Sensitive Individuals; Preliminary Experiments, J. Allergy **15:** 271 (July) 1944. Kolodny and Denhoff.[13d] Crieg.[13a]

18. (*a*) Lamb, J. H.: Allergic Reactions During the Administration of Penicillin, Arch. Dermat. & Syph. **52:** 93 (Aug.) 1945. (*b*) Crieg.[13a] (*c*) Price.[13c] (*d*) Kolodny and Denhoff.[13d]

19. McKlosky and Smith.[13b] Lamb.[18a]

20. Rostenberg, A., Jr., and Welch, H.: A Study of the Types of Hypersensitivity Induced by Penicillin, Am. J. M. Sc. **210:** 158 (Aug.) 1945.

21. (*a*) Pyle, H. A., and Rattner, H.: Contact Dermatitis from Penicillin, J. A. M. A. **125:** 903 (July 29) 1944. (*b*) Silvers, S. H.: Contact Dermatitis from Amorphous Sodium Penicillin, Arch. Dermat. & Syph. **50:** 328 (Nov.) 1944. (*c*) Barker, A. N.: Allergic Reactions to Penicillin, Lancet **1:** 177 (Feb. 10) 1945. (*d*) Michie, W., and Bailie, H. W. C.: A Case of Penicillin Reaction, Brit. M. J. **1:** 534 (April 21) 1945. (*e*) Goldman, L.: Cheilitis from Local Use of Penicillin Solution in the Mouth, Arch. Dermat. & Syph. **53:** 133 (Feb.) 1946. (*f*) Gottschalk and Weiss.[10a]

22. Gottschalk and Weiss.[10a] Rostenberg and Welch.[20] Cormia and associates.[15a]

23. Binkley, G. W., and Brockmole, A.: Dermatitis from Penicillin: Report of Two Cases, Arch. Dermat. & Syph. **50:** 325 (Nov.) 1944. Herrell and associates.[7b] Kolodny and Denhoff.[13d]

24. Green, H. J., and Hobby, G. L.: Transmission of Penicillin Through Human Placenta, Proc. Soc. Exper. Biol. & Med. **57:** 282, 1944. Hutter, A. M., and Parks, J.: The Transmission of Penicillin Through the Placenta: A Preliminary Report, Am. J. Obst. & Gynec. **49:** 663 (May) 1945.

25. Jadassohn, W.; Schaaf, F., and Wohler, G.: Analyses of Composite Antigens by the Schultz-Dale Technic: Further Experimental Analyses of Trichophytins, J. Immunol. **32:** 203 (March) 1937.

26. McDermott, W., in discussion on Penicillin, New York State J. Med. **45:** 1875 (Sept. 1) 1945. Crieg.[13a]

27. Hampton, S. F.; Wise, M. B.; Allen, W.; Thompson, C. S., and Starr, M. P.: The Clinical Use of Penicillin in the Treatment of Intrinsic Bronchial Asthma, J. A. M. A. **127:** 1108 (April 28) 1945. Vermilye.[12]

28. Gottschalk and Weiss.[10a] Cormia and colleagues.[15a]

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vascular system.[15a] Gottschalk and Weiss [10a] expressed the opinion that epidermal sensitizations do not predispose to dermal or vascular sensitization; however, severe systemic involvement was encountered in Cormia's [15a] patients following local application of penicillin. If local applications can produce generalized sensitivity, as seems possible, a word of caution should be made against the injudicious use of penicillin locally.

Allergic symptoms following penicillin therapy are usually mild, of low incidence and transient. Several authors have recommended that treatment be continued after their appearance and have minimized their seriousness.[29] Others are more cautious and have emphasized that heed should be given to these manifestations, as persistence with treatment might lead to severe, alarming and serious reactions.[30] Wile [31] considered that severe angioneurotic edema and edema of the pharynx, larynx and lungs, known to accompany penicillin therapy, are serious and may be fatal complications. Lamb [18a] expressed the opinion that each patient should be questioned regarding history of allergy, history of previous penicillin sensitivity and history of trichophytosis or other fungous infections. When a patient is sensitive to crystalline penicillin, as may be shown by cutaneous reactions or suspected when different lots or products of different manufacturers produce symptoms or give positive reactions, continued therapy should be used with extreme caution or only after desensitization, as severe reactions may be anticipated.[30b] Kolodny and Denhoff [10d] stated that dermatologic patients possess a higher sensitivity rate than other patients.

THERAPEUTIC SHOCK

Therapeutic shock or Jarisch-Herxheimer reaction symptoms incident to the therapeutic use of penicillin in the treatment of syphilis are frequently encountered [32] and are considered evidence of the efficacy of penicillin.[33] Focal reactions are manifested by intensified chancre and other cutaneous lesions within eight to twelve hours or delayed for days in tissues of low vascularity, as in osseous syphilis. If treatment is started in the seropositive primary stage, before objective symptoms other than serologic are present, a profuse secondary rash may develop. Systemic reactions produce malaise, generalized aching, painful adenopathy, chill and elevation of temperature to 103 F. The symptoms usually subside within twenty-four to forty-eight hours, and treatment may be continued without interruption. If symptoms do not subside within a reasonable time, production factors other than therapeutic shock must be considered.

A Herxheimer reaction can be avoided by early reduced dosage of penicillin. It should be avoided in certain types of syphilitic infections, as in those of debilitated or toxic persons,[7b] particularly infants,[29d] and in late syphilis, gummatous, cardiovascular [34] and that of the central nervous system.[35]

Therapeutic shock symptoms occurring during the routine treatment of gonorrhea in which syphilis is not diagnosed or suspected or before the serologic reaction becomes indicative are considered diagnostic or at least suggestive of concurrent syphilitic infection.[36] Fever following the use of purified penicillin is rare and should arouse a suspicion of a Herxheimer reaction and syphilis.[37] Calloway and associates [38] did not consider that divided early dosage prevents fever. Therapeutic shock symptoms have followed the treatment of syphilis with oral administration of penicillin.[39] The incidence of Herxheimer reactions is high, 86 per cent [40] and 91.6 per cent having been reported.

TABLE 2.—*Toxic Reactions to Penicillin Produced by Contact (Epidermal) Sensitivity*

Dermatitis (venenata): erythematous, circumscribed pruritic, mild, severe, vesicular, bullous, edematous, weeping, exfoliating	Cheilitis Conjunctivitis Scleritis Blepharitis Glossitis Edema of the penis and scrotum

TABLE 3.—*Penicillin Produces Therapeutic Shock Reactions*

I. Focal
Exaggeration of cutaneous lesions; increased swelling, redness and discharge of chancres; enlarged regional adenopathy; precipitation of secondary lesions; increased pain in bones

II. Systemic
Malaise, chills, fever, nausea, vomiting; urticaria, erythema multiforme, morbilliform and scarlatiniform erythema; hoarseness, dyspnea, aphysxiation; myelitis, pseudoencephalitic syndromes, cranial nerve injuries, convulsions, coma; exaggeration of lightning pains; hallucinations, mania; cardiac embarrassment, ruptured aneurysm

INDIRECT ACTION ON PATHOLOGIC PROCESSES

The harmful effects following penicillin therapy on pathologic processes, which Stokes [41] called "paradox reaction of healing" and "therapeutic paradox," should

29. (*a*) Cohen, T. H., and Pfaff, R. O.: Report of Results in One Hundred Cases: Penicillin in Dermatologic Therapy, Arch. Dermat. & Syph., **51:** 172 (March) 1945. (*b*) Stokes, J. H., and others: Penicillin in Late Syphilis: An Interim Report, Am. J. Syph., Gonor. & Ven. Dis. **29:** 313 (May) 1945. (*c*) Pillsbury, D. M.: Penicillin Therapy of Early Syphilis in 14,000 Patients: Follow-Up Examination of 792 Patients Six or More Months After Treatment, Am. J. Syph., Gonor. & Ven. Dis. **30:** 134 (March) 1946. (*d*) Lentz, J. W.; Ingraham, N. R., Jr.; Beerman, H., and Stokes, J. H.: Penicillin in the Prevention and Treatment of Conenital Syphilis: Report on Experience with the Treatment of Fourteen Pregnant Women with Early Syphilis and Nine Infants with Congenital Syphilis, J. A. M. A. **126:** 408 (Oct. 14) 1944. (*e*) Lyons,[28b] (*f*) Herrell and associates,[28c] (*g*) Rostenberg and associates,[29] (*h*) Cormia and associates.[15a] (*i*) Kolodny and Denhoff,[10d] (*j*) Feinberg.[37]

30. (*a*) Sullens, W. E.: Simulating Serum Sickness Reactions to Penicillin, U. S. Nav. M. Bull. **45:** 752 (Oct.) 1945. (*b*) Strozza, J. A.: Delayed Sensitization to Penicillin Similar to Serum Sickness, J. A. M. A. **130:** 1071 (April 20) 1946. (*c*) Price, D. E.; McNairy, D. J., and White, E. L.: Severe Asthma: Delayed Sensitization to Penicillin, J. A. M. A. **128:** 183 (May 19) 1945. (*d*) Morris, G. E., and Downing, J. G.: Bullous Dermatitis (Dermatitis Medicamentosa) from Penicillin, J. A. M. A. **127:** 711 (March 24) 1945. (*e*) Criep,[12a] (*f*) Price,[12c] (*g*) Kolodny and Denhoff,[10d] (*h*) Lamb,[18a] (*i*) Pyle and Rattner,[21a] (*j*) Barker.[21c]

31. Wile, U. J.: Editorial Remarks, Bull. Rapid Treat. Centers, U. S. Pub. Health Serv., January 1945, vol. 1, no. 4.

32. Mahoney, J. F.; Arnold, R. C., and Harris, A. D.: Penicillin Treatment of Early Syphilis: A Preliminary Report, Am. J. Pub. Health **33:** 1387 (Dec.) 1943.

33. (*a*) Neilson, A. W.; Chard, F. H.; Henchett, L. J.; Ayers, E.; Stepita, C. T., and Rodriquez, J.: Penicillin in the Treatment of Syphilis and Gonorrhea, South. M. J. **38:** 204 (March) 1945. (*b*) Ricchinti, J. F., and Brett, W. B.: Treatment of Gonorrhea with Penicillin in a Naval Dispensary, U. S. Nav. M. Bull. **45:** 520 (Sept.) 1945.

34. Delkert, R. E., and Schwemlein, G. X.: The Treatment of Cardiovascular Syphilis with Penicillin, J. A. M. A. **129:** 515 (Oct. 13) 1945.

35. Nelson, R. A., and Duncan, L.: Acute Syphilitic Meningitis Treated with Penicillin, Bull. Johns Hopkins Hosp. **75:** 327 (Dec.) 1944. Stokes, J. H.; Sternberg, T. N.; Schwartz, W. H.; Mahoney, J. F.; Moore, J. E., and Wood, W. B., Jr.: The Action of Penicillin in Late Syphilis, J. A. M. A. **126:** 73 (Sept. 9) 1944. Stokes and others.[29b]

36. Bauer, F. K., and Egolf, C. F.: Herxheimer Syndrome Following Penicillin in Unsuspected Syphilis, Bull. U. S. Army M. Dept. **14:** 239 (Aug.) 1945. Thomas, R. B., and Meyer, E.: Penicillin in the Treatment of Gonorrhea: Results with Six Hundred and Seventy-Five Women, Ven. Dis. Inform. **26:** 94 (May) 1945. Ricchinti and Brett.[33b]

37. Leifer, W., and Martin, S. P.: Effect of Penicillin on Course of Early Syphilis, J. A. M. A. **130:** 202 (Jan. 26) 1946.

38. Calloway, J. L.; Durham, N. C.; Noojin, R. O.; Flower, A. H., Jr.; Kuhn, B. H., and Riley, K. A.: The Use of Penicillin in the Treatment of Syphilis of the Central Nervous System: A Report on One Hundred Patients, Am. J. Syph., Gonor. & Ven. Dis. **30:** 110 (March) 1946.

39. Paul, W. D.; Rhomberg, C., and Wallace, E.: Penicillin by Mouth in Combination with Aluminum Dihydrooxyaminoacetate, J. Indiana M. A. **38:** 298 (Sept.) 1945.

40. Mahoney, J. F.; Arnold, R. C.; Sterner, B. L.; Harris, A., and Zwally, M. R.: Penicillin Treatment of Early Syphilis, J. A. M. A. **126:** 63 (Sept. 9) 1944.

41. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926.

be considered. In late syphilis of the heart, too rapid healing of a coronary lesion by penicillin may produce deforming sclerosis and atresia so rapidly that no compensation can take place. This is a different process and independent of cardiac embarrassment following acute local vascular edema of the Herxheimer reaction. "Rapid healing with fibrosis in the liver results either in a diffuse contraction or localized deformities which affect the patient by obstructing his portal circulation, with resultant ascites, or by producing severe intractable jaundice." [41] Divided and cautious early therapy with penicillin will permit some degree of physiologic adjustment.

REACTIONS FOLLOWING INTRATHECAL ADMINISTRATION

Apparently penicillin has a direct irritating effect when applied to the central nervous system, and this property is contained in penicillin and crystalline penicillin rather than in the impurities. Walker and Johnson [42] showed that seven commercial penicillins administered intracisternally, intraventricularly and locally to the cerebral cortex produced convulsions and death due to vascular collapse in mice, cats, dogs and monkeys and that intracortical injections produced convulsive seizures in human beings. One hundred thousand units in 20 cc. of isotonic solution of sodium chloride produced cyanosis, irregular respirations and convulsions with temperatures to 104 F. and signs of vascular collapse in an infant.[43] Neymann, Heilbrunn and Youmans [44] stated that penicillin is toxic when it comes in direct contact with the surface of the brain, producing, as acute effects, headache, tenseness, muscular twitching, convulsions and cyanosis and, as chronic effects, meningeal irritation, rigidity of the neck and positive Kernig and Brudzinski signs. All symptoms were reduced after diminished dosage and particularly with concomitant use of barbiturate sedatives.[42c] Intrathecal reactions are apparently due to high dosage rather than to concentration of the drug and are not due to acidity or alkalinity of the solution, as sodium chloride and 95 per cent alcohol did not reproduce the symptoms.[45] The convulsive factor is related to the antibiotic properties of penicillin rather than to impurities, as convulsive seizures diminished directly proportionally to the destruction of the antibiotic properties by aging, boiling and acidifying and by dissolving penicillin in alcohol.[42a] There is a species factor in convulsive effects, as the threshold for monkeys is lower than that for cats.[42a] Crystalline penicillin produced the same reactions when used intrathecally.[42c] Five thousand units applied to the occipital cortex in human beings showed no clinical or electroencephalographic abnormalities, whereas 20,000 units produced encephalographic changes. Application of 10,000 units to the motor area resulted in twitching of the face and hands for three hours.[42a]

TABLE 4.—*Reactions Following Intrathecal Administration of Penicillin*

Listlessness	Flaccid extremities
Headache	Stiffness of neck
Nausea	Convulsions
Vomiting	Comatose
Cold, clammy skin	Unconsciousness
Vascular collapse	Electroencephalogram changes
Irregular respirations	Spinal fluid cell count, globulin, albumin increased in nonsyphilitic patients
Cyanosis	
No blood pressure	
Thready pulse	Positive Kernig sign
Muscular twitching	Positive Brudzinski sign
Clonic spasms	

The convulsive effects of penicillin should not detract from its clinical intrathecal use when indicated, as the therapeutic dosage is usually below that which produces convulsions.[42c] A normal patient shows no reactions to doses from 3,000 to 5,000 units.[46] Patients have received from 20,000 to 100,000 units without reactions; however, the higher dosage should be used with caution.[47] Neymann, Heilbrunn and Youmans advised no dosage above 30,000 units.[44] It is noted that no reactions have been reported when penicillin is applied directly to wounds or abscesses in the central nervous system. This may be due to impaired diffusion of the drug through the walls of granulation tissue to adjoining nerve tissue.[42a]

From our present knowledge, reactions following administration of penicillin to the central nervous system are due to irritative, rather than allergic, therapeutic shock and paradoxic therapeutic reactions. Symptoms produced by these different types of reactions should not be confused.

CONCLUSIONS

1. Penicillin may produce reactions due to its action as (*a*) direct toxin and primary irritant, (*b*) antigen, (*c*) therapeutic shock excitant, and (*d*) indirect action on pathologic processes.

2. Salient observations concerning each action group are discussed.

3. Tables are presented listing toxic reactions encountered in each group.

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ABSTRACT OF DISCUSSION

DR. HAROLD M. JOHNSON, Honolulu, Hawaii: It is gradually being realized that penicillin is not an innocuous drug. Two years ago, statements were made regarding the lack of toxicity and sensitizing effect. Now it is common to see new cases in which the reactions are mild to severe. In cases of the severe reaction, patients have stated that they would rather have their previous infection than penicillin therapy. The usual allergic reactions are mild and transient. Parenteral therapy has been continued in these cases. In the contact eczematous reactions, therapy was immediately discontinued. Usually the person can tolerate a fever, headache and bone-joint pain, but the itching and burning of epidermal sensitization require quick removal of the preparation. In 1944 a large drug firm stated, "The untoward reactions early attributed to penicillin unquestionably were in direct proportion to the toxic impurities rather than due to the penicillin." Recent reports appear to refute this

42. (*a*) Walker, A. E., and Johnson, H. C.: Convulsive Factor in Commercial Penicillin, Arch. Surg. **50**: 69 (Feb.) 1945; (*b*) Intraventricular Penicillin: A Note of Warning, J. A. M. A. **127**: 217 (Jan. 27) 1945. (*c*) Walker, A. E.; Johnson, H. C., and Kallros, J. J.; Penicillin Convulsions: The Convulsive Effects of Penicillin Applied to the Cerebral Cortex of Monkey and Man, Surg., Gynec. & Obst. **81**: 692 (Dec.) 1945.

43. Simon, S. M.: Untoward Effects of Penicillin: Prophylactic Use in Spina Bifida Operations, Clin. Med. **52**: 87 (March) 1945.

44. Neymann, C. A.; Heilbrunn, G., and Youmans, G. P.: Experiments in the Treatment of Dementia Paralytica with Penicillin, J. A. M. A. **128**: 433 (June 9) 1945.

45. Rosenberg, D. H., and Arling, P. A.: Penicillin in the Treatment of Meningitis, J. A. M. A. **125**:1011 (Aug. 12) 1944. Walker and Johnson.[42a]

46. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Toxicity of Penicillin Administered by Intrathecal Injection, Am. J. M. Sc. **205**: 342 (March) 1943.

47. Worth, L. H.: Staphylococcal Leptomeningitis Treated with Intracisternal Penicillin, Lancet **2**: 634 (Nov. 17) 1945. Walker and Johnson.[42a]

statement somewhat. Now patients allergic to one brand are allergic to the administration of penicillin from another manufacturer. Penicillin, a complex organic formula, could have increased its sensitizing ability by the manufacturer's change to newer commercial penicillin. It is possible, as Dr. Morginson stated, that persons may be sensitive to penicillin because they possess a varied sensitivity to all molds. This may well be the explosive factor seen in the exacerbation of a previous fungous infection. It is believed that a substantial percentage of the population is sensitive to crystalline penicillin sodium despite the fact that these persons have had no previous contact with this material. Theoretically this mold is ingested or inhaled, producing in susceptible persons a mild reaction with later changes in their immunologic responses. A few simple rules may help prevent reactions, such as the reduced dosage during the first six to twelve hours or even twenty-four hours, depending on the urgency in the case. The importance of the Herxheimer reaction to penicillin is proportional to the physiologic importance of the tissue involved. It is suggested that the patient be questioned regarding previous history of eczema, especially seborrheic, personal or familial, and history of cutaneous hypersensitiveness and chronic urticaria. Nine times out of ten these questions are never asked. Much grief by the patient and the physician could be avoided. Benadryl and Pyribenzamine (N'pyridil-N'benzyl-N-dimethylethylenediamine) can be used to alleviate the urticarial serum sickness–like reaction. If given early a great amount of discomfort can be eliminated. The dosage of Benadryl must be high in the severe reactions and frequently repeated. The drowsiness encountered can be fairly well controlled by oral administration of amphetamine sulfate. In a small series of cases I have been able to avoid the described reactions by the prophylactic administration of Benadryl, 100 mg. three times daily, during parenteral therapy and ten days following the ceasing of penicillin therapy.

DR. BEN A. NEWMAN, Los Angeles: The cutaneous reactions caused by penicillin are particularly important since penicillin is being more and more prescribed for comparatively minor infections (and even noninfections) of the skin and mucous membranes. The sequence of events that precipitated the innumerable sensitizations during the past decade of sulfonamide therapy is already being duplicated. Those who served with large military hospitals were impressed with the low incidence of reactions to penicillin. Its use in the armed forces was chiefly limited to the sulfonamide-resistant pneumonias, to the more serious surgical or medical infections and to the treatment of syphilis and gonorrhea. Generally the patients had never received penicillin previously, and the reaction rate did not exceed 2 or 3 per cent. This is in accord with the earlier reports on the use of penicillin. On the other hand, in a group of patients I treated with penicillin for chronic infectious or eczematoid dermatoses the reaction rate exceeded 30 per cent. Although penicillin reactions from topical therapy in the acute infectious dermatoses have so far been minimal, I am willing to predict an increase in such reactions as more and more of the population are exposed to penicillin. Since my return to civilian practice, in addition to the many local contact dermatoses I have seen many instances of generalized urticarias, generalized erythemas and morbilliform rashes, vesicular eruptions and generalized eczematous eruptions from such use of the drug. Generally, these have occurred in patients who received penicillin in a previous instance. Experience among most dermatologists has shown that the use of penicillin externally in the form of an ointment or cream is of value only in the most superficial infections, that is, the impetiginous lesions. For deeper infections of skin or mucous membranes, topical applications are of limited value. The treatment of superficial impetiginous infections with topical application of penicillin does not appear to be superior to the therapies that have been used heretofore. Of even greater importance than cutaneous reactions from the topical use of penicillin is the probability that this usage of the drug will sensitize a large number of persons. Obviously, this is likely to prevent or complicate the administration of penicillin for serious systemic or organic infections. Penicillin is now available in the form of ointments, mouth washes, lozenges, lotions and first aid dressings as well as in the parenteral and oral forms. Its indiscriminate use for local infections of the skin and oral mucosa is to be condemned for the following reasons: first, the uncertain and questionable results over formerly established remedies; second, the potential hazard of sensitizing the patient to penicillin, and, third, the danger of precipitating untoward reaction in a previously sensitized patient.

COMMANDER E. E. BARKSDALE, Bethesda, Md.: I entirely agree with the author and congratulate him on a worth while presentation. I should like to report some observations made by the Penicillin Control Committee at the Naval Medical Center during the past four years, during which time over 20,000 patients received penicillin for one condition or another. Craig and the other members of the committee reported the observations on the first 2,000 patients treated early in 1944; no reactions were reported other than those observed as mild Herxheimer reactions occurring in the treatment of early syphilis. Such is not the opinion of the committee at the present time. It is our opinion that the over-all reaction rate of penicillin is approximately 8 to 10 per cent. I should like to report also one death from exfoliative dermatitis. The case will be reported in the literature. The man was not a syphilitic patient but a patient with cellulitis who had been previously sensitized to penicillin while at sea. When admitted to this hospital with cellulitis, we knew that he was sensitive, but he was also sensitive to sulfonamide drugs. He was given 100 units of penicillin every three hours. At the end of the seventh dose, administration of it had to be discontinued because of a severe cutaneous eruption which went into a generalized exfoliative dermatitis, streptococcic septicemia and death. In addition to what the author has reported, we have observed several cases of neuritis and have frequently had complaints of pain in the peroneal nerve. We have had 5 cases of complete foot drop. I do not think that this is an allergic reaction; exactly what it is we are unable to explain. Fortunately, all 5 cases of foot drop did clear up on physical therapy, but 2 of them took five months to do so. When we first thought of using penicillin in the skin department of the Naval Hospital at Bethesda, about 80 to 90 per cent of the patients on the ward were getting local penicillin in one form or another, either ointment or wet dressings. At present there is not one patient on local penicillin. In my opinion, penicillin locally in any form is absolutely contraindicated. I agree with Flippen of Philadelphia in that I think that penicillin locally can sensitize a person so that he cannot take it intramuscularly or otherwise. I see no advantage of the local application over the intramuscular injections, either in oil or in aqueous solution.

Okinawans.—These examinations were made at a military government hospital from June 13 to July 30, 1945. Death was due to combat injuries in 100 cases, to noncombat (chiefly medical) causes in 36 and to a combination of war injuries and medical conditions in 14. . . . The most striking finding was the low incidence of retrogressive and degenerative changes. Senility came late, and cardiac and skeletal muscles remained well preserved even in the aged. Arteriosclerosis also developed late and to a moderate degree or not at all, and its lethal sequels in the brain, the kidneys and the heart were never seen. Hypertensive cardiovascular-renal disease was not seen except for 1 case of the type associated with toxemia of pregnancy. In fact, heart disease of all types, including congenital, rheumatic, bacterial endocarditic, syphilitic, hypertensive and coronary arteriosclerotic, was uncommon or absent. Renal diseases of all types were rare. Although cirrhosis of the liver was common, disease of the biliary tracts, including cholelithiasis, was not. After the life of these people had been studied, two possible etiologic factors appeared outstanding in explanation of these observations. They were (1) a low tension, placid, although physically strenuous, life and (2) a simple, predominantly vegetarian diet.—Steiner, P. E.: Necropsies on Okinawans, *Arch. Path.*, October 1946.

Special Article

HISTORY OF THE AMERICAN MEDICAL ASSOCIATION

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Editor, Journal of the American Medical Association and Hygeia, the Health Magazine
Chicago

(Continued from page 854)

(NOTE.—*Following is the sixth chapter of a history of the American Medical Association, in process of development for publication in connection with the celebration of the Centennial of the American Medical Association in Atlantic City in June 1947.*

The general account of the history of the Association will be followed by individual histories of the various councils, bureaus, publications and other activities of the Association. The general account is written by the editor of THE JOURNAL. *Each of the other historical contributions will be by a member of the individual council, bureau or agency responsible and now associated with it or directly related to its work. Included will be photographs, signatures and a brief biography of each of the hundred presidents of the American Medical Association. This feature has been prepared by Dr. Walter L. Bierring.*

It will be impossible to publish all of the material in THE JOURNAL. *The complete work will be published in book form. It is hoped to have it available by the time of the annual session.*—ED.)

CHAPTER 6. 1849-1852

1849

BOSTON

In the amphitheater of the Massachusetts General Hospital in 1846 Dr. John Collins Warren had done the first public operation under ether anesthesia. At the meeting of the American Medical Association in 1849, held in Boston, he served as chairman of the committee of reception of the Massachusetts Medical Society; he was nominated President of the American Medical Association for the ensuing year. Whether or not there was any direct association between these facts there is, of course, no way to determine. The Association was still holding its sessions by a technic which involved the formation of special committees on such subjects as surgery, forensic medicine, indigenous botany and hygiene, but the primary interest was still the reform in medical education. The convention reiterated its approval of the resolutions on this subject adopted by the convention that met in Philadelphia in 1847. The attention of all the medical colleges was called again to the report on preliminary education. Already some agencies were endeavoring to find a substitute for clinical instruction in the hospital; a resolution was offered that the Association did not sanction or recognize college clinics as substitutes for hospital clinical instruction.

Significantly it was now agreed that state medical societies should be formed in every state in which they did not exist and that the societies should admit to their membership only those who had obtained degrees in medicine and had been licensed by a recognized licensing body.

Progress was made also in the resolution which encouraged all the schools of medicine to meet at Cincinnati before the next annual meeting of the American Medical Association and to present a plan for elevating the standard of medical education. These were the preliminary steps toward the high standard that was ultimately to prevail in the advancement of American medicine.

An innovation was the establishment of standing committees to undertake measurement of progress in each important medical field. To this resolution were appended the words "giving special attention to such as may be American." The committees included a Committee on Arrangements, Anatomy, Physiology, Materia Medica, Chemistry, Pathological Anatomy, the Principles and Practice of Medicine, of Surgery and of Obstetrics, Hygiene and Sanitary Measures, Forensic Medicine, Medical and Vital Statistics, American Medical Biography, Medical Education and Publication. These subjects of main interest were to be modified from time to time with the progress of medical science and with the advancement of knowledge in each of these specialties. Gradually anatomy, physiology, chemistry and pathology were to be directed for their scientific considerations primarily to special societies formed specifically for such purposes. Hygiene and sanitary measures, which were particularly the problem of the medical profession, were to be absorbed in the great field of public health administration. Medical and vital statistics became functions eventually of the Bureau of Census and the U. S. Public Health Service. American medical biography was to be merged gradually into the Directory of the American Medical Association. But in this formative stage each of these topics was considered of equal interest with every other; there was but one organization to give proper consideration to all of them.

Rather amusing in view of the present stage of medical education in the United States was the submission by the faculty of medicine of Harvard to the Committee on Medical Education of an elaborate defense of the limitation of the courses of medical instruction in the schools to four months—a limitation seriously opposed by the committee itself. A committee was appointed to prepare at leisure a statement of the facts and arguments which may be adduced in favor of prolonging the courses to six months.

Well in advance of their time also were resolutions indicating that the state medical associations in east Tennessee and New York had developed a series of popular lectures designed to enlighten the public mind in relation to the new position of medical men in relationship to society; it was urged that the American Medical Association recommend medical men in all associations, individually, by public lectures and otherwise, "to enlighten the public mind in regard to the duties and responsibilities of the medical profession and their just claims to the confidence of the public." Eighty years later the continuing demand for suitably informing the public caused the formation of a division of public relations in the American Medical Association.

Although but two years had passed, many members were beginning to get a little weary of the length of time required to read the annual reports. Their attention was called to the fact that the constitution merely required them to report on the progress of medicine in this country alone and only during the year of their service.

Realize too that, although the time was almost a hundred years ago, a resolution was offered requesting the Committee on Practical Medicine to inquire into the expediency of adopting the English language exclusively in the writing of prescriptions and in all

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directions for the composition and administration of medicines. This reform has still not reached the stage of majority approval.

These in the year 1849 were the chief interests of the American Medical Association from the point of view of its social, political and economic relationships. The reports of its special committees, however, merit at least a word because of some extraordinary interests. There was a report on the anatomy of the dodo, supposed by some to be a fictitious creation. It seemed, however, that the British *Forensic Medical and Chirurgical Review* of the previous year had published a report that this bird was not fictitious but that it was instead a massive and clumsy bird and that "we cannot form a better idea of it than by imagining a young duck or gosling enlarged to the dimensions of the swan." An investigator was convinced that there was no free hydrochloric acid in the gastric juice, and another insisted that there is nothing whatever to phrenology. Cholera was the major epidemic disease, and a gynecologist was treating dysmenorrhea by dilating the cervix of the uterus. A woman in Kentucky tried to poison her baby by giving it powdered glass, and another woman sued the doctor sixteen months after the baby was born because "he had placed hands upon her person." This action resulted from reading a book which was an attack on male obstetricians. There were extensive reports on the use of ether for anesthesia and a conclusion that all the accidents from anesthesia in the United States had resulted from the inhalation of chloroform. There had been 13 deaths from anesthesia by use of surgeons, 2 by dentists and 2 by people who had breathed chloroform for its pleasurable reactions. Typhoid raged rather widely, as did also an epidemic of streptococcic sore throat called angina, and several outbreaks of dysentery and intestinal disturbances. Cerebrospinal meningitis appeared in epidemics in a good many places, as did yellow fever.

The Committee on Surgery concerned itself also chiefly with anesthesia. Dr. J. Mason Warren had operated in a case of imperforate anus, but the progress of surgery was minute indeed. The Section on Obstetrics was chiefly concerned with misplacements of the uterus, but there was an extensive discussion on ovariotomy, which was spoken of as "this tremendous operation."

There are pages devoted to the right of the physician to use an anesthetic in labor. To this the committee wisely concluded that, "in the more severe obstetric operations, not only may anesthetics be rightfully given but they may not be rightfully withheld."

Extensive indeed was the report of the Committee on Medical Education, which offered a survey of medical education in the countries of Europe and a comparison of their education with the education offered in each of the medical schools of the United States. The continuous publication of such analyses of medical education has been one of the most potent factors in raising the standard of medical education in the United States.

The interest in public health caused the publication in the Transactions of that year of an analysis of the sanitary conditions in many of the most important cities and areas in our country. These pages constitute a source book for those interested in the progress of public health. The report from New Orleans is especially interesting in its attack on inebriety as a means of injury to the public health but more particularly in its endorsement of health education. In presenting the sanitary report of New Orleans, Dr. Edward H. Barton twice repeated the statement of Benjamin Rush that the medical profession was from twenty to thirty years ahead of the public in information in relation to health and that it required about that amount of time for the public to become sufficiently enlightened to realize the value of hygienic laws, observances and improvements.

Reports on drugs and indigenous botany occupied hundreds of pages which would be of little practical value to the physician of today with his specific synthetic chemotherapy.

One consideration for the Association was the question as to whether or not the introduction of water and gas into cities should be under the control of private agencies or municipal agencies.

As the convention came to its close, Dr. Thomas Wood presented a resolution requesting the Committee on Medical Science "to inquire into the expediency of establishing a board to analyze the quack remedies and endorsement now palmed upon the public and to publish the results of their examinations in a newspaper to be established for the purpose; and, further, to append such plain views and explanations thereto as will enlighten the public in regard to the nature and dangerous tendencies of such remedies."

1850

CINCINNATI

The year 1850 saw the convention moving as far west as Cincinnati, and an Ohio physician, Dr. Reuben D. Mussey, was chosen President.

The earlier resolutions on education had begun to bear fruit. A resolution of thanks was tendered to the faculties of the University of Pennsylvania and to the College of Physicians and Surgeons of New York and to all "other institutions which may have conformed to our recommendations." But medical education was still the most troublesome problem. One resolution demanded that young men be not admitted to medicine unless they had good moral character and had exhibited evidence of a good education. Daniel Drake amended this to demand "that the medical schools of the United States should require pupils to remain till the end of the session, whatever may be its length, except when permission may be given to depart," indicating that a good many boys who enrolled departed when the harvesting season or some other similar project demanded their presence elsewhere. Health education of the public was still a desirable object, and Dr. Austin Flint suggested that a popular address on some medical subject should be annually delivered at this Association before the citizens of the place in which the meeting is held. A few scientific papers were read, one the exhibition by Dr. Evans of Chicago, then professor of obstetrics in Rush Medical College, of a device which he called an obstetrical extractor, which he demonstrated on a manikin, and another by Nathan Smith Davis with the peculiar title "Has the Cerebellum Any Special Connection with the Sexual Propensity of Function of Generation?" This proved that there is nothing scientific about phrenology.

A resolution was passed condemning the clerical profession for "often—though, perhaps sometimes, unwarily—yielding their extensive influence in the community in giving currency to quackery and quack medicines."

Again in advance of public opinion and the times, another resolution proposed "that this Association regard it as contrary to its system of ethics for medical journals to advertise nostrums or secret remedies although their composition may have been made known to the editor."

The Association urged its support to the international copyright law. The Committee on Publications again recommended that the medical profession create its own medical literature rather than be subservient to that of England.

A group welcomed the action of the government which proposed to confer military rank on medical officers of the Army.

The meeting, being in Cincinnati, the Transactions are obviously a little less in scope and quantity than those of meetings held in the East nearer the great centers of population.

The Committee on Medical Literature called attention to the fact that a good many editors had already withdrawn to other departments of professional labor, some had tired of their ill paid toils and thankless duties, and some had been snatched away by the hand of death. For each of these losses the committee expressed its sense of bereavement. Already there were complaints that there were too many medical journals. The committee felt that the average value would be enhanced were the quantity reduced one half. Some of the medical journals, it seemed, had been established by gentlemen connected with medical schools and for the purpose mainly of sustaining the latter. Although the journals published at a distance from great medical centers were uniformly weak, the committee thought that they ought to be encouraged since their difficulties to exist were so great. The committee felt also that "it speaks but feebly in praise of our physicians as scientific investigators, that there are but two experimental memoirs of any importance contained in the journals of the last year." Incidentally one of these dealt with the actions of poisons and the other with the nervous system of the alligator.

Indeed the annual analysis of the medical literature of the day, which had come to be a regular feature at meetings of the American Medical Association, was significant in the gradual improvement in its quality. There is an essay on the functions of the critic or reviewer which might well be an inspiring text to any one essaying that thankless task in modern times. Analyzing the books that had been published in the previous year, the committee felt that the most extensive and important was the first volume of Dr. Daniel Drake's "Treatise on Diseases of the Interior Valley of North America." Incidentally, as an appendix to the report there is a complete bibliography of original articles of interest published in American journals between May 1849 and May 1850.

There follow the usual analyses of medical literature and of medical progress in a variety of fields, with a notable essay by J. Collins Warren on the use of anesthetics. This pointed out that already in his amphitheater in the Massachusetts General Hospital more than a thousand etherizations had been done without an unfortunate result. The introduction of anesthesia had permitted surgical operations not previously possible. J. Collins Warren reported also a number of operations for the removal of cancers and other tumors.

1851

CHARLESTON, S. C.

The fourth annual meeting convened in Charleston, S. C., in 1851. Dr. Alfred Stillé, who had served as secretary of the Association and who had written the memorable report on literature of the previous year, had been compelled to tender his resignation because his health had forced him to seek relaxation abroad.

Conspicuous among those who gave direction and impetus to the work of the American Medical Association during the formative years was Dr. Alfred Stillé of Philadelphia. Dr. Stillé was the son of Swedish emigrants, a graduate of Yale University in 1832 and of the University of Pennsylvania with an A.M. in 1835, the M.D. in 1836 and the LL.D. in 1839. Following his graduation in medicine he became house physician at Blockley under W. W. Gerhard. In association with Gerhard, he is credited with being among the first to make a clear distinction between typhoid fever and typhus. The great epidemic of typhus in Philadelphia in 1836 gave him opportunity for many postmortem examinations which permitted him to make a clear distinction between the two conditions and ultimately to convince the British physicians who had refused to accept such a distinction. In 1854 he became professor of the practice of medicine in the Pennsylvania Medical College, and in 1864 he succeeded the first Dr. Pepper in the chair of medicine at the University of Pennsylvania. He was the first secretary of the American Medical Association, and he was rewarded with the presidency in 1867.

Sir William Osler knew him well, but only after Stillé had passed his seventieth year. Of him Osler wrote "He had none of those irritating features of the old doctor, who, having crawled out of the stream about his fortieth year, sits on the bank, croaking of misfortunes to come, and, with less truth than tongue, lamenting the days that have gone and the men of the past." In his valedictory address Stillé said "Only two things are essential; to live uprightly and to be wisely industrious."

The representative session was largely concerned with whether or not to admit delegates from dentistry and pharmacy into the convention, with an attempt by the Congress to repeal the law that it had passed conferring military rank on military physicians, and with continuing emphasis on the improvement of medical education.

A variety of special committees were suggested to investigate special diseases as well as epidemics. Another committee was established to receive volunteer communications and to offer a prize for the most meritorious. This year the versatile Dr. Davis read a paper on an experimental inquiry concerning the processes of assimilation and nutrition.

For those interested in budgets, the annual expenditures of the Association amounted to $1,100. Since there was a slight surplus in the treasury, some of it was made available for publishing. The prizes for the most meritorious essays came from fifty dollar gifts made by Dr. Alfred Stillé and Dr. F. G. Smith.

1852

RICHMOND, VA.

Richmond got the meeting for 1852, and in due course a Virginia physician, Dr. Beverley R. Wellford, became President. The society adopted a resolution admitting a delegate from the American Medical Society of Paris.

Dr. Austin Flint of Buffalo won the prize for the most meritorious essay out of sixteen voluntary com-

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munications. The subject of his essay was "On Variations of Pitch in Percussion and Respiratory Sounds, and Their Application to Physical Diagnosis." The essay received, incidentally, the unanimous vote of the committee.

This year the scandal in transportation of steerage passengers from Europe to the United States attracted the attention of the Association. The following resolution was introduced:

> The accumulation of passengers who are emigrants, crowded in ships coming to our shores from foreign ports, having in a great many instances numerous cases of aggravated fever, many of which prove fatal, and likewise producing similar results at the lazarettos, and even cities; the number, likewise, of sick arriving from California, and some of the South American ports, and the fact that none of these vessels are required by law to have physicians or surgeons on board, seem deserving of our attention as conservators of health, and as an act of humanity and duty on the part of the American Medical Association, to bring these facts respectfully to the consideration of Congress, and to request its legislation thereon; Be it therefore
>
> *Resolved*, That the American Medical Association do memorialize Congress to require all vessels carrying steerage passengers on the sea to have a surgeon on board.
>
> *Resolved*, Further, that a committee of this Association be appointed to draw up a memorial to Congress, making such suggestions as it may deem fit as regards the importance of this measure.

Now there arose also some complaint of doctors not connected with the faculties of the medical schools against the monopolization of practice by the teachers. A resolution was offered suggesting that "it be considered unethical to operate upon the legitimate patient of any other physician, knowing that to be such and that the possible perversion of clinics to the private emolument of those conducting them should be scrupulously guarded against."

A committee was set up to declare the contents of a medicine chest for a merchant ship and the directions that ought to go along with it.

There were new attacks on the quality of medical education and defenses by those who were for the status quo. There were amendments to the constitution and by-laws, with an interesting suggestion that the University of Virginia should be entitled to representation in the Association, notwithstanding the fact that it did not have six professors and that it did not require three years of study.

Some twenty-seven essays had been offered to the committees that were to award the prizes. There came a resolution that one prize of $250 be awarded instead of five prizes of $50 each, but another amendment that there be two prizes of $100 each prevailed.

A good many papers were read by title and offered to the publication committee.

Incidentally the resolution giving special courtesy to the University of Virginia prevailed "but only so long as the present peculiar system of instruction and examination practiced by that institution shall continue in force."

This year the income of the Association doubled but so did its expenditures, so that there was left in the treasury the sum of $56.75.

What had been going on elsewhere in the world that should perhaps have attracted more attention at the assemblages of the American Medical Association than seems to have been given?

In France, Claude Bernard was making fundamental discoveries year after year. In 1848 he had discovered the glycogenic function of the liver. In 1849 he had produced diabetes by puncture of the fourth ventricle, and in 1851 he had explained vasomotor functions of the sympathetic nerves.

In 1844 Addison had described pernicious anemia and adrenal disease. Helmholtz had measured the velocity of the nerve current, and several surgeons had operated to relieve abscess of the brain. The hypodermic syringe was invented in 1852 by Pravaz, and little was it realized how frequent would be its use at the end of one hundred years. In 1853 the Crimean war apparently stirred little interest in the meetings of the American Medical Association, but that was the war in which Florence Nightingale founded the profession of nursing. Today questions of nursing are at the very forefront of all considerations in the field of medical care.

The year 1855 saw the introduction of the laryngoscope by Manual Garcia. The Bunsen burner was invented. J. Marion Sims founded a hospital for women's diseases in New York City. Perkins developed the aniline dyes as coal tar products in 1856; from this first step came such remedies as the salicylates, aspirin and eventually arsphenamine and the sulfonamides. Then in 1857 Graefe introduced his operation for strabismus; Bouchut performed intubation of the larynx.

The operation described by J. Marion Sims in 1852 was the result of a number of discoveries beginning in 1845 which involved the development of the peculiar lateral posture known as the Sims position, the invention of the special curved speculum, the use of silver wire for sutures and of the catheter for emptying the bladder while operating on the uterus. The monumental paper of Sims was published in 1852 in the *American Journal of the Medical Sciences* in Philadelphia. It created a profound impression throughout the world. In 1853 he moved to New York, where he founded the hospital for women, which soon became the center of the best gynecologic work of its time. Such procedures were already beginning to add fame to the progress of medicine in America.

Perhaps the most significant book in these first ten years following the founding of the American Medical Association was Daniel Drake's work on "Diseases of the Interior Valley of North America." As pointed out by Fielding Garrison, this was the result of thirty years of labor based largely on personal observation. The first volume is an encyclopedia of the geography, topography, climate, plants and animals and population of the Mississippi Valley; the second volume, an account of malaria and other fevers and of the various epidemics in their relation to the geography, meteorology and topography of the area concerned. This was the first work of its kind since the treatise of Hippocrates on "Airs, Waters and Places" but went even beyond Hippocrates on its relation of epidemiology to geography. When Alfred Stillé reported on it at the meeting of the American Medical Association in 1850, Drake was greeted with prolonged and thunderous demonstrations of applause and enthusiasm such as had been seldom accorded to any American physician previously. Dr. John Shaw Billings reports that "he covered his face with his hands and wept like a child." Daniel Drake, as described by S. D. Gross, was a tall, commanding figure, simple and dignified in manner. "He was always well dressed, and around his neck he had a long gold watch-chain, which rested loosely upon his vest." He lectured with a splendid voice and with fiery eloquence.

(To be continued)

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Clinical Notes, Suggestions and New Instruments

A PROTECTIVE WRAPPING FOR THE ANKLE

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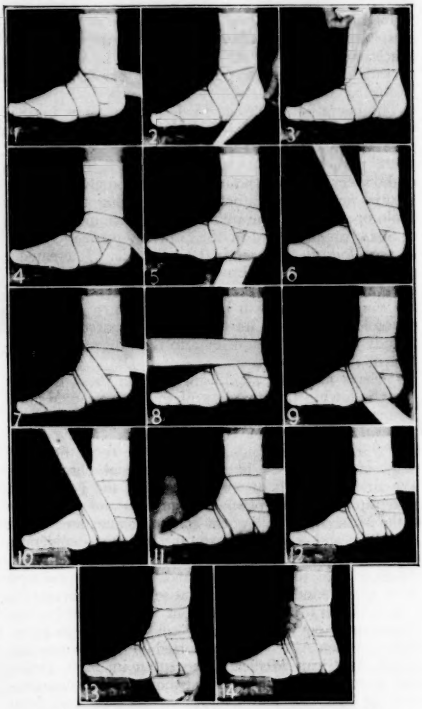
and
JOSEPH MURPHY
Boston

The vulnerability of the ankle has long been known to athletes and trainers, and protective bandaging is commonly practiced. The usual wrapping consists of turns taken in a "figure 8" fashion around the malleoli and foot, crossing at the anterior aspect of the astragalus. When critically examined, this bandage really accomplishes little; neither lateral nor anteroposterior motion is greatly limited, and little protection is afforded against sprain or fracture.



Steps (1 to 14) in application of protective ankle wrapping.

For the past fifteen years at Harvard College every student who participates in contact sport has been taught a method of wrapping the ankle which considerably limits lateral motion without interfering appreciably with flexion or extension. During this period, not one player wearing this wrapping has suffered a complete rupture of an ankle ligament. When sprains do occur they are minor, and the average period of disability, before return to full athletic participation, has been only eight days.

A considerable number of former college athletes, having learned to apply the wrapping as undergraduates, have used it enthusiastically on weekend skiing expeditions. With the growing popularity of winter sports and the high incidence of injuries to the ankle among amateur skiers and skaters, a description of the method seemed worthy of publication.

Bandages are cut to 100 inch (254 cm.) lengths from 2¼ inch (5.7 cm.) nonelastic ribless muslin tape and thoroughly shrunk by washing in extremely hot water before use. The wrapping is applied over the inner of two pairs of smoothly fitting socks. The toes are placed on the edge of a chair, and the ankle is held firmly at an angle of 90 degrees. The end of the bandage is placed at the lateral malleolus and unrolled snugly, without wrinkles, over the proximal end of the first metatarsal, across the sole, upward, crossed at the center of the ankle joint and back over the medial malleolus (1 in the illustration).

At this point it is angled sharply downward across the lateral aspect of the os calcis, carried across the sole, upward on the medial aspect of the foot and over the lateral malleolus (2, 3 and 4). Again it is angled sharply downward, this time over the medial aspect of the os calcis, carried across the heel and up around the medial malleolus (5, 6 and 7). The remaining turns are of the "figure 8" type around the tarsus and ankle at and just above the malleoli (8 to 14 inclusive). A "figure 8" turn of 1 inch (2.5 cm.) adhesive tape anchors the final turns.

SUMMARY

A protective wrapping for the ankle, for use by college athletes and others, is described. It can be applied by the athlete himself and reduces the incidence and severity of sprains of the ankle by limiting lateral mobility at the ankle joint without interference with flexion and extension.

From the Department of Surgery, Harvard Medical School, and the Medical Department, Harvard Athletic Association.

MASSIVE HEMATURIA DUE TO DICUMAROL OVERDOSAGE

DAVID ROSENBLOOM, M.D., and JAY J. CRANE, M.D.
Los Angeles

Dicumarol (3, 3'-methylene-bis-[4-hydroxycoumarin]) is the active principle in spoiled sweet-clover hay which causes hemorrhagic disease in cattle, and it is now made synthetically.[1] Physiologically, it suppresses thrombin formation [2] and impairs clot retraction,[3] and should be administered only if daily determinations of prothrombin time are made.[2] The usual dosage is given as 200 to 300 mg. initially, followed by 100 to 200 mg. a day orally. A twenty-four to forty-eight hour lag (sometimes five days [4]) is followed by an increase in the prothrombin time, and the normal time of 12 to 14 seconds [5] should not be permitted to increase beyond 35 to 60 seconds.[3] Daily prothrombin times should be taken, and preferably the patient should be hospitalized. After withdrawal of the drug, complete recovery takes six to ten days.[4] Overdosage is usually followed by bleeding from various sites of the body. Cohan [6] reported purpura after 2,800 mg. in thirty-two days had been given for postoperative emboli; hematuria persisted eight days after the withdrawal of Dicumarol, and a prolonged bleeding time with definite prothrombin deficiency was present, but platelet reduction or clot retraction abnormality was not observed.

1. Campbell, H. A.; Roberts, W. L.; Smith, W. K., and Link, K. P.: Studies on Hemorrhagic Sweet Clover Disease, J. Biol. Chem. **136**: 47 (Oct.) 1940.
2. Pfeiffer, D. B., and Sain, F. D.: Heparin and Dicumarol: Collective Review, Internat. Abstr. Surg. **78**: 109, 1944; in Surg., Gynec. & Obst., February 1944.
3. Allen, E. V.; Barker, N. W., and Waugh, J. M.: Preparation from Spoiled Sweet Clover [3,3'-Methylene-bis-(4-Hydroxycoumarin)] Which Prolongs Coagulation and Prothrombin Time of Blood, J. A. M. A. **120**: 1009 (Nov. 28) 1942.
4. Lucia, S. P., and Aggeler, P. M.: Treatment of Dicoumarol-Induced Hypoprothrombinemic Hemorrhage with Vitamin K_1 Oxide, Proc. Soc. Exper. Biol. & Med. **56**: 36 (May) 1944.
5. Todd, J. C., and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods, ed. 10, Philadelphia, W. B. Saunders Company, 1943, p. 201.
6. Cohan, A.: Hemorrhage and Purpura Caused by Dicoumarin, New England J. Med. **228**: 820 (June 24) 1943.

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Zucker,[7] in 18 cases in which an initial dose of 300 mg. of the drug was followed by daily doses of 200 mg. observed in 1 patient on the fourth day, a petechial rash of the upper extremity with a concomitant microscopic hematuria of 30 erythrocytes; 4 other patients had microscopic hematuria. Pfeiffer and Sain [2] have observed microscopic hematuria. Lucia and Aggeler [4] reported hematuria on the tenth day of Dicumarol administration (for thrombophlebitis) persisting to the seventeenth day, accompanied by epistaxis, ecchymoses at the sites of hypodermic injections and at herpetic lesions on the lip. Inquiries of several urologists in this city have elicited at least 2 instances of gross hematuria, both of which were definitely attributable to the ingestion of Dicumarol for thrombophlebitis.

Treatment of hematuria caused by Dicumarol consists of discontinuance of the drug, the administration of multiple blood transfusions,[8] and the administration of vitamin K_1 oxide [9] in large amounts (500 or more milligrams). Ordinary synthetic vitamin K is considered to be of little value,[10] although Smith and Kaufman [11] have employed it.

REPORT OF CASE

S. D., a man aged 32, was seen in consultation on Sept. 7, 1945. He stated that when he arose on the morning of Sept. 2, 1945 he had found fresh blood, which had apparently come from his gums, on the pillow; later in the day he had observed gross massive hematuria, so that the urine looked like "pure blood." His physician had made a diagnosis of "nephritis" and had put him to bed on a milk diet. Because of diffuse abdominal pain, an additional diagnosis of "ulcer" was made. One day before the onset of the hematuria, varicose veins in each leg had been injected with sodium morrhuate.

When we saw the patient, the urine was deeply bloody. Careful physical examination failed to demonstrate any abnormalities other than diffuse abdominal guarding and tenderness, and pronounced tenderness of the lumbar and renal area. Masses were not palpable, and normal peristaltic sounds were heard. Slight bleeding of the gingival margin also was present. He was hospitalized on Sept. 8, 1945, and hematologic studies demonstrated a bleeding time of 14 minutes, clotting time of 7½ minutes and a prothrombin time of 112 seconds. Examination of the blood revealed that erythrocytic, leukocytic, thrombocytic, and differential counts were within normal limits. An abdominal roentgenogram did not show calculi or other abnormalities of the urinary tract. The nonprotein nitrogen was 26 mg. per hundred cubic centimeters. At this time the patient was thoroughly requestioned and the history was elicited that in the seven days preceding Sept. 1, 1945, the day of the varicose vein injections, he had taken 46 capsules; the dispensing pharmacist was consulted and stated that the capsules each contained 50 mg. of Dicumarol. Therefore, 2,300 mg. of Dicumarol had been ingested within seven days.

The patient was immediately placed on a regimen of 40 mg. of synthetic vitamin K every two hours for six doses, followed by similar doses every six hours, and vitamin C, 250 mg., every six hours. Vitamin K_1 oxide was not obtainable. Strict rest in bed was enforced. However, the gross hematuria and abdominal pain did not diminish. A transfusion of 500 cc. of citrated blood was administered on September 10, and the procedure was repeated on September 11; on September 12 the hematuria began to lessen. On this day, the patient suffered six severe bilateral renal colics, requiring multiple injections of morphine for relief. These were interpreted as the passage of blood clots down each ureter. On September 13 the temperature suddenly rose to 102 F., and the fever was attributed to a transfusion reaction, postcolic mild pyelonephritis or ureteral trauma. He was given penicillin, 20,000 units every three hours, and sulfadiazine and sodium bicarbonate, 1 Gm. of each, four times a day. The fever promptly subsided, and by September 14 the urine was grossly clear. The patient was dismissed on September 15, afebrile and with clear urine. He was seen on September 16; he felt "washed out" but otherwise normal, and a voided specimen contained only an occasional erythrocyte when viewed microscopically. On September 22, a complete hematologic study was within normal limits. The prothrombin time was 14 seconds. An excretory urogram showed a normal urinary tract.

SUMMARY

A 32 year old man received 2,300 mg. of Dicumarol in seven days (approximately three and a half times the normal dose). Two days later, massive hematuria appeared. Synthetic vitamin K therapy was ineffective. Cessation of bleeding followed the transfusion of 1,000 cc. of blood.

COMMENT

In the differential diagnosis of hematuria, Dicumarol (3, 3′-methylene-bis-[4-hydroxycoumarin]) administration should be considered. The patient should be questioned about recently ingested drugs.

7. Zucker, H. D.: Clinical Experiences with Dicoumarol, J. A. M. A. **124**: 217 (Jan. 22) 1944.

8. Pfeiffer and Sain.[2] Lucia and Aggeler.[4]

9. Davidson, C. S., and MacDonald, H.: True Vitamin K Oxide in Treatment of Dicoumarol Overdosage, New England J. Med. **229**: 353 (Aug. 26) 1943. Shapiro, S.; Redish, M. H., and Campbell, H. A.: Effect of Vitamin K upon Hypoprothrombinemia Induced by Dicoumarol in Man, Proc. Soc. Exper. Biol. & Med. **52**: 12 (Jan.) 1943. Lucia and Aggeler.[4]

10. Allen, Barker and Waugh.[3] Lucia and Aggeler.[4]

11. Smith, E., and Kaufman, J.: Use of Dicoumarol and Vitamin K in Urological Cases, J. Urol. **52**: 353 (Oct.) 1944.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following report. HOWARD A. CARTER, *Secretary.*

OTARION MODEL A-4 JR. HEARING AID (SINGLE PACK) ACCEPTABLE

Manufacturer: Otarion Hearing Aid Company, 448 North Wells Street, Chicago.

This single pack hearing aid is a three tube instrument with transmitter and batteries in a pigskin leather case. A four position tone control lever is at the top of the case, and the combined on-off switch and volume control are on the side of the case. A magnetic type receiver is supplied with this instrument. The Otarion Model A-4 Jr. Hearing Aid is convertible, since it may be worn as a single pack (with transmitter and batteries in a single case) or with a separate battery case or pack in the conventional manner.

Dimensions: The case measures 1 by 2 9/16 by 5¼ inches (2.54 by 6.60 by 14.6 cm.).

Weight: The case (containing batteries and transmitter), receiver and cord weigh 9 ounces (255 Gm.).

Current consumption: A battery (1½ volts), 65.0 milliamperes, B battery (30 volts), 0.6 milliampere.

	Maximum Acoustical Gain						
Frequency	250	500	1000	2000	3000	4000	5000 cycles/second
Tone control							
White	27.5	33.5	39.0	42.5	34.5	26.5	14.0 decibels
Black	26.5	33.5	42.5	50.0	45.0	38.5	26.0 decibels
Green	21.0	28.5	39.0	47.5	43.5	37.0	25.0 decibels
Red	14.0	23.5	34.0	43.5	40.0	34.0	23.0 decibels

With the tone control at the white dot position the high frequencies are attenuated. In the black position the instrument reproduced with maximum width of frequency range. In the green position the low frequencies are moderately attenuated, and in the red position the high frequencies are attenuated maximally.

Performance: The instrument operates in an entirely satisfactory manner. There is a minimum of inherent noise. The pigskin leather case produces a slight amount of frictional noise, which is not perceptible when the transmitter is worn as a separate unit with a separate battery case.

The Council on Physical Medicine voted to include the Otarion Model A-4 Jr. Hearing Aid (Single Pack) in its list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 14, 1946

STREPTOMYCIN IN INFLUENZAL MENINGITIS

The mortality rate in Hemophilus influenzae meningitis was until recently above 92 per cent. Following the introduction by Alexander [1] of rabbit serum containing antibody against type B organisms, which she employed in combination with sulfadiazine, a reduction in the mortality rate to 26 per cent in a group of patients ranging in age from 3 months to over 5 years was reported.[2] In experiments on mice, Alexander and Leidy [3] demonstrated that streptomycin alone was more effective against massive H. influenzae infections in mice than serum used in conjunction with sulfadiazine. The results of treating 25 patients [4] who had H. influenzae meningitis of type B with streptomycin alone or in conjunction with serum and with serum and sulfadiazine suggest that streptomycin alone will bring about complete recovery when the infection is of mild or average severity. In 9 of the 12 patients who recovered on streptomycin therapy the spinal fluid cultures proved sterile twenty-four hours after initiation of streptomycin therapy, in the other 3 after forty-eight hours. The return to normal of the chemical constituents of the spinal fluid was equally rapid. Now Alexander recommends administering all three agents initially: streptomycin, type specific antiserum and sulfadiazine.

Logan and Herrell [5] employed streptomycin, sulfonamides and antiserum in the treatment of 4 infants suffering from H. influenzae meningitis. In 2 of these clinical and laboratory evidence of improvement did not occur until streptomycin was used. Three patients recovered. In the fourth, H. influenzae was eliminated from the cerebrospinal fluid after treatment with streptomycin, but the patient died several weeks later as a result of hydrocephalus. Weinstein [6] reported recovery in 8 out of 10 cases of purulent meningitis caused by H. influenzae of type B in 8 and by an untypable strain in 2. Streptomycin was given intramuscularly in doses ranging from 15,000 to 125,000 units every three hours and intrathecally in amounts varying from 10,000 to 25,000 units every twenty-four hours. Two of the 9 patients with influenzal meningitis treated with streptomycin died. One showed complete absence of response to the antibiotic agent. The other died of an intercurrent Staphylococcus aureus bronchopneumonia which was not affected by penicillin. The blood and spinal fluid were cleared of the causative organism in twenty-four to forty-eight hours in all cases except the 2 due to atypical strains. Relapses or sequelae were not observed in any of the recovered patients in six to ten weeks after the cessation of streptomycin treatment.

Of the 8 patients with H. influenzae meningitis treated by Birmingham and his associates [7] 4 recovered, 3 died and in 1 streptomycin therapy was given up in favor of sulfonamide and serum. Death in 1 case was associated with the appearance of drug fastness. Toxic reactions included erythema, urticaria, increase in meningeal signs, persistence of pleocytosis, local pain on injection and mild shock on initial administration. None of these were serious. Nussbaum and his associates [8] treated 3 children less than 2 years old with streptomycin intramuscularly and intrathecally and sulfadiazine, with recovery without complications or sequelae.

Further lowering of the mortality rate and lessened incidence of complications and sequelae may be accomplished by early diagnosis and initial employment of the three therapeutic measures streptomycin, the antibody rabbit serum and sulfadiazine. In any event the physician is no longer confronted with a hopeless prognosis in this meningeal infection.

1. Alexander, Hattie E.: Type B Anti-Influenzal Rabbit Serum for Therapeutic Purposes, Proc. Soc. Exper. Biol. & Med. **40:** 313 (Feb.) 1939.

2. Alexander, Hattie E.; Ellis, Catherine, and Leidy, Grace: Treatment of Type Specific Hemophilus Influenzae Infections in Infancy and Childhood, J. Pediat. **20:** 673 (June) 1942.

3. Alexander, Hattie E., and Leidy, Grace: Influence of Streptomycin on Type B Hemophilus Influenzae, Science **104:** 101 (Aug. 2) 1946.

4. Alexander, Hattie E.: Streptomycin in Pediatrics, J. Pediat. **29:** 192 (Aug.) 1946.

5. Logan, G. B., and Herrell, W. E.: Streptomycin in the Treatment of Influenzal Meningitis of Children, Proc. Staff Meet., Mayo Clin. **21:** 393 (Oct. 16) 1946.

6. Weinstein, Louis: Treatment of Meningitis Due to Hemophilus Influenzae with Streptomycin, New England J. Med. **235:** 101 (July 25) 1946.

7. Birmingham, J. R.; Kaye, Robert, and Smith, Margaret H. D.: Streptomycin in the Treatment of Influenzal Meningitis, J. Pediat. **29:** 1 (July) 1946.

8. Nussbaum, Sydney; Goodman, Solomon; Robinson, Clarence, and Ray, Louis: Influenzal Meningitis, J. Pediat. **29:** 14 (July) 1946.

MYTH AND MUMPSIMUS IN MEDICINE

"Myth and Mumpsimus," by Forbes,[1] concerns iconoclastic attitudes toward accepted beliefs and dogmas. Although medicine is not an exception, myth and mumpsimus have a way of lingering because of mental inertia and faith in traditional custom. "Mumpsimus" stands for "a traditional custom, obstinately adhered to however unreasonable it may be." It is a corruption of sumpsimus, first person plural indicative perfect of the Latin verb *sumo*, I take. With regard, for example, to the traditional forcing of fluids on patients with or without pyrexia in the hope of "aiding in the elimination of toxins," what is objected to is not the rationale

1. Forbes, J. R.: Myth and Mumpsimus, Lancet **2:** 293 (Aug. 31) 1946.

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of the procedure of replacing the loss of body fluids in a sweating febrile patient but the conception of the body as some sort of "involved water-closet to be cleansed by flushing with copious drafts of imperial drink." The ritual purgation in acute food poisoning and administration of magnesium sulfate in infective hepatitis "to promote the free flow of bile" are evidently based on misconceptions of the pathogenesis of these disorders.

Forbes is probably correct in stating that we do not have reason to think that diet is of any real importance in those diseases which are not associated with gastrointestinal dysfunction or with a definite upset of metabolism. He believes that the enforced disappearance, due to rationing and food shortage in England, of dietary regimens in the last few years has not led to any appreciable increase in death or disease. He thinks rather that many patients are the better for it. His peptic ulcer patients did not relapse any more frequently since he ceased to recommend a carefully selected diet for six months or longer, and he now merely advises them to eat within reason whatever food they find does not disagree. His patients seem to be better because they no longer feel obliged to consider their stomach before all else and to debate the digestibility of each dish before them. Physiologists will probably agree that appetite, when not perverted by gluttony or hysterical inhibitions or falsely determined by injudicious medical advice, is a reliable guide to what is and what is not good for a sick person. The forced overeating of patients with normal appetites, as was formerly practiced on consumptive persons, is in his opinion as foolish as undereating. The custom is disappearing, but its place threatens to be filled by the habit of indiscriminate prescription of vitamins. The medical profession in the United States will subscribe to the statement that the mythical healing properties attributed to vitamins by now far exceed their very real ones.

Prolonged immobilization of older patients, contributing as it does to the dangers of venous thrombosis and passive pulmonary congestion, is being discarded in favor of early ambulation. The same tendency to limit prolonged absolute rest is evident in the treatment of coronary thrombosis. The psychic damage to the person caused by the indiscriminate use of either correct or erroneous medical terms is not sufficiently appreciated by the profession. Forbes questions whether it is wise to inform our symptomless hypertensive patients of the state of their blood pressure. A young man with a functional systolic murmur, who gives a history of ten days of "rheumatism" in childhood, whose mother died of some vague "heart trouble" and who shows an inverted T wave in the third lead of his electrocardiogram, is almost certain to be diagnosed some time as having rheumatic heart disease, though he probably is normal and healthy. Such a diagnosis may have a devastating effect on a suggestible youth, leading to a cardiac neurosis which may result in a life of useless semi-invalidism. The author believes that such an error is at least as great as that of failing to detect a carcinoma in a man of 60. The number of outworn beliefs and practices is naturally multiplied in the field of drugs.

An iconoclastic attitude which insists on experimental and clinical demonstration of the validity of any practice is the surest antidote against myth and mumpsimus.

METHEMOGLOBINEMIA AND TISSUE OXYGENATION

Methemoglobin is a derivative of a normal respiratory pigment, produced by the action of various compounds among which are chlorates, nitrites, acetanilid, nitrobenzene, sulfonal and sulfanilamide. Whereas the oxygenation of hemoglobin produces a derivative (oxyhemoglobin) from which oxygen is readily eliminated under the conditions existing in the tissues, methemoglobin is relatively stable in the body and does not release its contained oxygen for purposes of tissue respiration. As the proportion of methemoglobin increases in the circulation, hypoxia develops and cyanosis appears. The increased incidence of methemoglobinemia following the use of sulfonamide drugs and the suggested therapeutic use of methemoglobin in the treatment of cyanide poisoning raise the question as to how far the favorable action of this derivative can be evoked without interfering with tissue oxygenation.

A recent report[1] describes experiments on human subjects. Relatively untrained as well as trained young men worked on a bicycle ergometer. The initial increase in concentration of lactic acid in the blood together with the subsequent removal was used as an objective index of oxygenation of the muscle. Comparison of the data secured in control periods with those obtained after part of the circulating hemoglobin had been changed to methemoglobin (oral administration of p-aminopropiophenone[2]) permitted conclusions regarding the effect of the altered respiratory pigment on tissue oxygenation. When 8 to 17 per cent of the blood pigment had been changed to methemoglobin, little if any effect on the rate of removal of lactic acid after exercise was noted in relatively untrained men. However, when the proportion of the oxidized pigment was increased to 22 per cent, there was definite evidence for the interference with muscle oxygenation after measured light exercise. Training for the mechanical work seemed to minimize the deleterious influence of methemoglobin on the oxygenation of muscle. However, when the severity of the work was increased the trained subjects, gave indication of impaired oxidative removal of lactic acid from the blood.

The evidence cited points to definite limits of concentration of methemoglobin in the circulating blood

1. Tepperman, Jay; Bodansky, Oscar, and Jandorf, B. J.: Am. J. Physiol. **146**: 702 (Aug.) 1946.
2. Vandenbelt, J. M.; Pfeiffer, Carl; Kaiser, Margaret, and Sibert, Margaret: J. Pharmacol. & Exper. Therap. **80**: 31 (Jan.) 1944.

beyond which there is interference with tissue oxygenation. Analytical methods for the quantitative estimation of this pigment are available, and information based on their use should be a reliable guide to management of patients in situations which promise to be somewhat more common.

Current Comment

POSTGRADUATE COURSES FOR PHYSICIANS

Semiannually the Council on Medical Education and Hospitals of the American Medical Association publishes lists of postgraduate courses offered to physicians throughout the country for the ensuing six months. In this issue of THE JOURNAL the course listings cover the period from Jan. 1, 1947 to July 15, 1947. With the increasing demand for such work from physician veterans there has been a continued increase in the number and variety of offerings. In the current listing there are approximately eight hundred courses offered by about ninety institutions and organizations, which is by far the largest number yet published for any six month period. The medical schools take a prominent part in presenting these courses. Forty-three schools will participate in the presentation of over five hundred courses. In addition a number of the courses, while not given by a medical school, will employ the facilities of medical schools. The wide usefulness of these listings is evidenced by the tremendous demand for reprints. Institutions and individuals participating in these programs are rendering a great service to the profession and to the physician veterans. THE JOURNAL and the Council are indebted to them for making publication of the lists possible.

RECENT ADVANCES IN HUMAN GENETICS

Penrose [1] recently analyzed the familial data in 144 cases of anencephaly, spina bifida and congenital hydrocephaly. The data comprised 137 sibships, which were selected on the basis of at least one child affected with the three congenital conditions mentioned. In seven of these sibships a second case of one or other of the conditions occurred. Statistical calculations were made which showed that advancing maternal age bore a significant relationship to the incidence of this group of malformations. When maternal age was eliminated as a factor by statistical means, primogeniture was shown to have some probable etiologic significance. The first of these tentative conclusions conforms with opinions expressed by Murphy [2] and others in this country. In the same issue of the *Annals of Eugenics* Harris [3] has presented what amounts to a scientific study of the commonly made statement that some families run principally to boys or principally to girls. His report is based on a family of watchmakers in England whose family tree could be accurately traced since 1690. During this period thirty-five children were born into the family, of which only two were girls. Harris said that there is small probability of such a sex ratio occurring by chance and that therefore the hypothesis that some hereditary tendency is at work would appear reasonable. An examination of the seminal fluid was made on one representative of this family. In number, percentage, motility and percentage of abnormal forms the spermatozoa were within the usual normal limits. Definite microspermatozoa, that is, smallness in size of the sperm heads, was found. Consequently Harris suggests that there may be a genetic interconnection between individual relative sexual inactivity (as in the case of the man in question), spermatozoa of unusually small head lengths and a family showing a tendency to infertility and the propagation of predominantly male progeny.

1. Penrose, L. S.: Familial Data on 144 Cases of Anencephaly, Spina Bifida and Congenital Hydrocephaly, Ann. Eugenics **13**: 73 (Aug.) 1946.
2. Murphy, Douglas P.: Congenital Malformations, Philadelphia, University of Pennsylvania, 1939.
3. Harris, H.: Microspermia in an Individual Form of Family of Unusually High Sex Ratio and Low Fertility, Ann. Eugenics **13**: 156 (Aug.) 1946.

THROMBOSIS AND EMBOLISM IN SWEDEN

Zilliacus [1] has recently summarized the results of treatment in 1,158 cases of deep venous thrombosis and pulmonary embolism in twenty Swedish clinics from 1940 to 1945. Comparisons were made of conservative treatment, heparin therapy and Dicumarol (3-3′-methylene-bis-[4-hydroxycoumarin]) therapy. Deep venous thrombosis or sudden pulmonary embolism occurred in 646 (0.51 per cent) of 125,524 surgical patients, 387 (0.40 per cent) of 96,672 obstetric and gynecologic patients and 125 (0.37 per cent) of 34,086 medical patients. Pulmonary embolism developed in 44 per cent of the surgical and 22 per cent of the obstetric patients with deep venous thrombosis. Calculated on the total number of patients admitted, the incidence of pulmonary embolism was 0.23 per cent, with mortality rates of 0.105 per cent in surgical cases, 0.011 per cent for obstetric and gynecologic cases and 0.053 per cent for medical cases. Of 214 cases of deep venous thrombosis of the leg treated conservatively, the thrombosis spread to the thigh in 4 out of 5. In contrast, it was confined to the lower part of the leg in approximately half of 576 patients given specific anticoagulant therapy. Of patients who received the best attention as to early diagnosis and treatment, the thrombosing process was confined to the calf in 4 out of 5. In 30 per cent of the conservatively treated group the thrombosis spread to the other leg, whereas this occurred in only 1.4 per cent of those in whom specific therapy was applied. A striking absence of late sequelae was noted in those patients in whom the acute thrombotic process was restricted to the lower part of the leg. Of 282 cases of sudden pulmonary embolism death occurred in 114 within such a short time that opportunity was not afforded for specific treatment. However, in contrast to 21 deaths among 65 patients treated conservatively, there was no mortality in a group of 103 patients who received anticoagulants (71 with heparin, 16 with heparin and Dicumarol and 16 with Dicumarol alone).

1. Zilliacus, H.: On the Specific Treatment of Thrombosis and Pulmonary Embolism with Anticoagulants, with Particular Reference to the Post-Thrombotic Sequelae, Acta med. Scandinav. **171**: 1, 1946.

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ORGANIZATION SECTION

Official Notes

THE ATLANTIC CITY SESSION

Applications for Space in the Scientific Exhibit to Close January 13

The Committee on Scientific Exhibit of the Board of Trustees has authorized four special exhibits for the Atlantic City session: Fractures, Physical Medicine, Heart Disease and Fresh Pathologic Material. Each exhibit will be presented by a special committee assisted by a large group of demonstrators.

In addition to the special exhibits, each section of the Scientific Assembly will present groups of exhibits dealing with the various specialties of medicine. Applications for space in these section exhibits are now being received and will close on January 13. Application blanks may be obtained from the section representatives or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10.

Washington Letter

(From a Special Correspondent)

Dec. 9, 1946.

Top Scientists Sought for Federal Service

Arthur S. Flemming of the U. S. Civil Service Commission informed the annual meeting of the Association of Science Teachers that the government plans to increase its cooperation with colleges and universities to develop scientists and other professional men for positions in the federal service. He said it was essential that government laboratories be staffed with scientists who were "second to none," and he advocated raising the federal pay ceiling from $10,000 to $15,000 annually to attract and retain persons of the highest caliber.

Socialized Medicine Criticized

John H. Hayes, president of the American Hospital Association, told the Maryland-District of Columbia Hospital Association that socialized medicine was an experiment which would cost more in taxes and salary deductions than present hospital care. He stated that if the present charitable work of physicians, community chest agencies and others were matched by a government subsidy, the amount would "stagger even a Congressman." Socialized medicine, he said, would result in poorer medical care, increased public debt and heavier salary deductions.

New Facilities Aid Research on Common Cold

Dr. R. E. Dyer, director of the National Institute of Health at Bethesda, Md., announced that new facilities will be put to work in a study of the common cold, part of a broad gage research program to see what science can do to prevent and cure this common malady. Colds keep an average of 250,000 people absent from their work daily, according to a U. S. Public Health Service survey. This research is part of the comprehensive attack by the institute on the principal diseases afflicting human beings.

The C. I. O. Will Seek More Health and Welfare Features in Contracts

Following the report by THE JOURNAL that the American Medical Association approved "cooperative health planning by management, labor and medicine, provided scientific and ethical standards are maintained," the C. I. O. announced that it planned to endeavor to incorporate more health and welfare features in union contracts. An extremely favorable stand toward the editorial position of THE JOURNAL was noted in several governmental sources.

International Exchange of Students as Step to World Peace

Professor Robert Andrew Milliken, Nobel prize winner of the California Institute of Technology, declared that the most hopeful prospect for world peace is to stimulate the exchange of teachers and research workers between countries. He was one of several noted speakers attending a convocation and reception at the National Museum commemorating the hundredth anniversary of the Smithsonian Institution. Also present were delegates from the National Academy of Sciences, the American Philosophical Society and various foreign scientific organizations, including the British Royal Society and the Institute de France. Dr. L. P. Eisenhart, executive director of the American Philosphical Society, and Dr. Frank B. Jewett, president of the National Academy, brought greetings to the institution. Dr. Vannevar Bush, president of the Carnegie Institution of Washington, presided as representative of the Smithsonian board of regents.

Millionth Baby Born with Birth Expenses Paid by Government

The Federal Security Agency announced that during the past week the millionth baby was born somewhere in the United States whose birth expenses were paid by the Emergency Maternity and Infant Care program of the Children's Bureau. The program, now in its fourth year, is administered by health departments of the states. Wives and infants under 1 year of men serving in the lowest grades of the Army, Navy, Coast Guard and Marine Corps are eligible for care at government expense without regard to family circumstances or racial status. All costs of doctor, nurses and hospitals are paid by the government. At one time the government was paying for between 40,000 and 45,000 maternity cases a month, but the number is down now to about 15,000 a month.

UNRRA Grants Funds to World Health Organization

The United Nations Relief and Rehabilitation Administration has given to the embryonic World Health Organization interim commission a credit of $1,500,000 to carry out UNRRA's health activities, beginning January 1 in Europe and next April in China. The interim commission, meeting in Geneva November 4 to 13, authorized its executive secretary, Dr. Brock Chisholm, to use up to $500,000 of the UNRRA credit in the first quarter of 1947. By a vote of 36 to 0 the Social, Humanitarian and Cultural Committee of the United Nations asked the assembly to recommend that all members ratify the World Health Organization constitution.

Infantile Paralysis Declines in Nation, Attacking 489 During Week

Infantile paralysis was reported by the U. S. Public Health Service to be declining in the nation during the past week, when it afflicted 489 men, women and children, bringing the total of cases up to 23,427 for this year. There were 13,514 cases all of last year and 19,053 in 1944, the worst poliomyelitis year since 1916. The 1946 toll is expected to reach 25,000.

Producers of Streptomycin Ask Removal of Controls on Distribution

The Civilian Production Administration has been asked by the producers of streptomycin to relax distribution controls in order to make larger supplies available to users.

Coming Medical Meetings

American College of Surgeons, Cleveland, Dec. 16-20. Dr. Dallas B. Phemister, 40 E. Erie St., Chicago 11, Secretary.

Southeastern Allergy Association, Atlanta, Ga., Jan. 18-19. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

GOVERNMENT SERVICES

ARMY

NEW COURSE IN PREVENTIVE MEDICINE

A new course in elementary preventive medicine has been opened at the Medical Department Professional Service Schools, Army Medical Center, Washington, D. C., in order to provide preventive medicine officers for the immediate needs of the Army. The five weeks course will consist of lectures, field work and laboratory investigations. The present class comprises 51 students, 34 of whom are newly appointed medical officers. Sixteen Air Corps doctors are in the group. There is one representative from the Ecuadorian army, Capt. Efrain Z. Guerrero.

While much of the instruction will be carried out by the staff of the Army Medical Center and Walter Reed General Hospital, distinguished civilian doctors will lecture as part of the plan in appointing specialists as consultants to the Secretary of War. Among them will be Kenneth Maxcy, Johns Hopkins University; John H. Dingle, Western Reserve University Medical School, Cleveland; Thomas Francis, University of Michigan School of Public Health; Henry M. Thomas, Johns Hopkins University; Martin Frobisher, Johns Hopkins University; Esmond Long, Phipps Institute, Philadelphia; Joseph Stokes, University of Pennsylvania; George Larrimore, National Cancer Research Foundation, New York; John B. Youmans, Vanderbilt School of Medicine; Albert B. Sabin, University of Cincinnati, and Clarence S. Livingood, University of Pennsylvania.

ARMY EPIDEMIOLOGICAL BOARD RECEIVES AWARD

The Army Epidemiological Board was one of five groups in the fields of medical research and public health administration to receive the Lasker Group Award during the annual meeting of the American Public Health Association in Cleveland in November. Dr. Francis G. Blake, dean, Yale University School of Medicine, New Haven, Conn., chairman of the board during the time for which it was cited, accepted the award on behalf of the board. The Army Epidemiological Board was cited for its work in the control of infectious diseases, one aspect of which was its development of an effective vaccine against influenza. In addition to the services of some 125 authorities on infectious diseases, the board enlisted the facilities of some universities and scientific institutes and conducted extensive surveys and experiments in all theaters where American troops were in operation.

Other groups awarded were the Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture; the National Institute of Health, U. S. Public Health Service; the Northern Regional Research Laboratory, Department of Agriculture, and the Board for the Coordination of Malarial Studies. The latter board was composed of representatives of the Army, Navy, Public Health Service, National Research Council, Committee on Medical Research and other civilian organizations engaged in malaria research.

IODINE INSTEAD OF CHLORINE FOR WATER PURIFICATION

A new tablet for purifying water in the soldier's canteen which is considered superior to the chlorine type tablets used during the war, has been announced by the War Department. The new tablet makes the drinking water less objectionable in taste and odor, can be used under a wider range of conditions, and dissolves more quickly than its predecessor. Scientists of the Army Medical Department, Quartermaster Corps and Corps of Engineers, after examining a large number of different compounds, found that triglycine hydroperiodide possessed the best military characteristics. Quickly dissolving tablets containing this chemical, which liberated 7½ parts per million of elemental iodine, were subjected to extensive testing and were found to be safe and highly effective.

Additional tests of the new "tablet, water purification, individual, iodine," as the compound has been designated, will be carried out during the ensuing year.

ARMY AWARDS AND COMMENDATIONS

Colonel John E. Elmendorf Jr.

The Legion of Merit was recently awarded to Col. John E. Elmendorf Jr., M. C., A. U. S., New York, for exceptionally meritorious conduct in the performance of outstanding services as director of the Army School of Malariology from Jan. 14, 1944 to June 3, 1945 and as commandant of the Army School of Malariology from June 4, 1945 to Jan. 25, 1946. The citation states that "his energetic application of foresight, inventiveness, organizing ability and leadership was of inestimable value to the organization's smooth function and constant improvement of the school. Through his intimate and profound knowledge of Central America and his courteous and dignified professional manner, Colonel Elmendorf has been able to obtain the active cooperation of Alcalded, Corregidores, public health nurses and school teachers in the interior towns of the republic of Panama to carry on malaria surveys and to secure teaching material for the classes attending the Army School of Malariology and to maintain the most cordial relations with the residents of the towns in which the tests were carried out. Colonel Elmendorf's sound judgment, initiative and cheerful attitude under most trying conditions reflect the highest credit to himself and the military service." Dr. Elmendorf graduated from the Johns Hopkins University School of Medicine, Baltimore, and entered the service Dec. 18, 1943.

NUTRITION LABORATORY

Dr. Robert E. Johnson became technical director of the Army Medical Nutrition Laboratory at Chicago on October 1, succeeding Dr. George H. Berryman. Dr. Johnson, who holds a Ph.D. from Oxford and an M.D. from Harvard, has been associated with the Harvard University Fatigue Laboratory since 1935 and has done much research in the field of physiology and nutrition. Dr. Berryman, who holds a Ph.D. from the University of Minnesota, was commanding officer and director of the nutrition laboratory from its activation in 1941 until he left, October 1, to attend the University of Illinois Medical School.

DIRECTOR OF LIBRARY SERVICE APPOINTED

Mr. Francis R. St. John, who during the war was acting librarian at the Army Medical Library and later was chief of the circulation department, New York Public Library, has been appointed director of library service for the Veterans Administration effective Jan. 1, 1947. Mr. St. John will direct the work of more than 150 libraries scattered throughout the United States.

LIBRARIAN RESIGNS

Mr. Wyliss E. Wright has resigned as librarian of the Army Medical Library to become librarian of Williams College, Williamstown, Mass., effective Jan. 1, 1947. Mr. Wright came to the Army Medical Library in 1945 from the New York Public Library, where he was chief cataloguer. From 1930 to 1933 he was librarian at the American Academy in Rome.

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CHARGE FOR PHOTODUPLICATION SERVICE

The Army Medical Library, which during the war conducted a free photoduplication and microfilm service on a global basis in the interest of medical research, will make a nominal charge for this service starting Jan. 1, 1947. The volume of this work had increased so much that a revision of policy was recommended by a committee studying the matter under the auspices of the honorary consultants at the request of the Surgeon General. This move will also place the library in line with other federal agencies which charge for similar services. The following price scale has been set up:

Microfilm.—Periodical Articles: A flat charge of 50 cents for any article in a single volume. Books and Serial Publications: Fifty cents for each fifty pages or fraction thereof.

Photoprints.—Fifty cents for each ten pages or fraction thereof from any single volume.

Method of Payment.—All charges are on the basis of cash with order. Only federal agencies are exempted from this requirement. Payment may be made by cash or by check or money order drawn to the Treasurer of the United States.

Order blanks are available on request.

PERSONAL

Brig. Gen. Raymond W. Bliss, Deputy Surgeon General, is making a six weeks tour of army medical installations in Europe. Last year General Bliss inspected all army medical installations in the Pacific Theater, and last spring he returned to Bikini for the atomic bomb test.

PUBLIC HEALTH SERVICE

STANDARDS OF HOSPITAL CONSTRUCTION

The Hospital Survey and Construction Act, authorizing a nationwide program of hospital construction, requires that standards of construction and equipment be established by the Surgeon General, U. S. Public Health Service. These standards will apply to all projects to be built with federal assistance under this legislation.

Such standards have recently been drafted by the Office of Technical Services, Division of Hospital Facilities, U. S. Public Health Service, of which Marshall Shaffer is chief. The Committee on Hospitalization and Public Health of the American Institute of Architects approved the standards and submitted them to a special technical committee on architectural standards appointed by the Federal Hospital Council.

This committee, which met in Washington November 12 and 13, includes in its membership James R. Edmunds, president, American Institute of Architects, chairman; Dr. Claude Munger, director, St. Luke's Hospital, New York; Dr. Frank F. Tallman, Committee of Mental Hygiene, Department of Public Welfare, Ohio; Dr. Warren P. Morrill, Director of Research, American Hospital Association; Dr. Ralph Horton, director, Homer Folks Tuberculosis Hospital, Oneonta, N. Y.; William A. Riley, architect, Boston, and A. N. Langius, director, Building and Construction Division, State Administrative Board, Michigan.

After review and approval by this committee, the standards were accepted by the Federal Hospital Council. These standards will be incorporated in the rules and regulations of the Hospital Facilities Division. The Surgeon General and the federal security administrator will have to approve the rules and regulations before they are published and made available to all persons interested in this program. It is hoped that they will be ready before December 31.

The standards established constitute the minimum requirements considered necessary to insure properly planned and well constructed hospitals and health centers. But since they are minimum requirements, it is pointed out that they should form a basis only for the development of higher standards.

There has been no attempt, in establishing these standards, to make them coincide with all the various state and local codes and regulations. However, strict compliance with all applicable state and local regulations is required. Likewise, compliance is required with minimum standards of construction and equipment promulgated by the state agency administering this program, where such standards are higher than those established by the Surgeon General.

In general, these standards fall into five classifications: site, architectural, structural, mechanical and drawing and specifications. The architectural standards cover the following types of projects: general, tuberculosis, mental psychiatric and chronic disease hospitals; nurses' homes; schools of nursing; public health centers, and state public health laboratories. The mechanical standards cover heating, steam piping and ventilation; plumbing and drainage; electrical; elevators and dumbwaiters; refrigeration; kitchen equipment, and laundry.

DEDICATION OF MEMORIAL LABORATORY

The recent dedication of the new Memorial Laboratory for the study of infectious diseases was attended by medical and civilian dignitaries of the United States, Russia and China. The laboratory, the eighth building of the National Institute of Health at Bethesda, Md., is this country's expression of gratitude for the sacrifices of the twenty-three members of the United States Public Health Service who have died in line of duty. The first of these martyrs was Dr. Roswell Waldo, who succumbed to yellow fever in 1878. Three names were inscribed on this roll of honor as recently as 1944: those of Dr. Richard G. Henderson, fatally infected with scrub typhus, bacteriologist Rose H. Parrott, who died of tularemia, and scientific aide Philip LeRoy Jones, fatally infected with scrub typhus.

The three story brick building, built at a cost of $1,500,000, will be the scene of intensive research on various virus and rickettsial diseases. The building has been planned and constructed to provide maximum safety for the scientists who will carry on this dangerous work. Dr. Charles Armstrong, chief of the Division of Infectious Diseases, National Institute of Health, will administer the new laboratory.

At the ceremony the director of the National Institute of Health, Dr. Rolla E. Dyer, welcomed the more than three hundred guests and introduced the speakers, including Dr. Thomas Parran, Surgeon General, United States Public Health Service; Dr. James Crabtree, Deputy Surgeon General; Dr. Detlev Bronk, chairman, National Research Council; Dr. Vassily V. Parin, secretary general, Academy of Medical Science of the U. S. S. R., and Dr. Szeming Sze, representative, National Health Administration of China.

OFFICERS COMMENDED BY NAVY

Comdr. E. G. Williams and Lieut. Comdr. Howard L. Andrews, both of the U. S. Public Health Service, have been commended by Vice Admiral W. H. P. Blandy, commander, Joint Task Force One, for work in connection with "Operation Crossroads." Commander Williams' assignment called for procurement of radiation detection instruments and radiation sources, which project Admiral Blandy characterized as most difficult. Commander Williams was also praised for establishing the "technical exercise," or instrumentation phase, of the training course. Lieutenant Commander Andrews assisted Commander Williams and also served as instructor in physics and nuclear physics. The admiral declared that Andrews was outstanding in this assignment. Admiral Blandy wrote that the "fine capabilities, initiative, cooperative attitude, technical knowledge and leadership displayed by these officers make them a real credit to the service."

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Gift to University Eye Clinic.—The Alabama Sight Conservation Association recently donated $10,000 to the department of ophthalmology of the Medical College of Alabama to provide equipment for the University Eye Clinic. The association was organized April 2, 1944 by the Alabama Lions Clubs, and its funds are derived from club memberships, life memberships, case memberships, contributing memberships and individual memberships; the East-West baseball game played each June in Birmingham sponsored by the Birmingham *News-Age Herald, Esquire* magazine, Alabama Lions and Alabama Sight Conservation Association, Inc.

CALIFORNIA

Personal.—Dr. Frank H. Rodin has resigned as ophthalmologist to the bureau of child hygiene, San Francisco Department of Public Health, a position he held for twenty years. He has been succeeded by Dr. Thomas G. Hall, San Francisco, who graduated at St. Louis University School of Medicine in 1923.——Dr. Norman Reider, Los Angeles, has been appointed chief of the psychiatric clinic at Mount Zion Hospital, San Francisco, to succeed the late Dr. Jacob S. Kasanin, San Francisco.

Cancer Fund Honors Dr. Lynch.—The Frank Worthington Lynch Memorial Fund for Cancer Research was recently established as a perpetual memorial fund to Dr. Lynch, who at the time of his death was professor of surgery and gynecology. The fund will finance special research in the history of cancer started by Dr. Lynch some thirty years ago. Dr. Herbert F. Traut, professor of surgery and gynecology and successor to Dr. Lynch, is in charge of continuing the research under the fund. Other sponsors are Dr. George Ebright, associate clinical professor of medicine emeritus, and Dr. William B. Thompson, Los Angeles.

COLORADO

Dr. Masten Goes to Oregon.—Dr. Alfred R. Masten, Denver, director, division of tuberculosis control, Colorado State Board of Health, Denver, has been appointed to the administrative staff of the Oregon State Board of Health, Portland, newspapers announced October 8.

Dr. Gengenbach Made Professor Emeritus.—Dr. Franklin P. Gengenbach, Denver, has been appointed professor emeritus of pediatrics at the University of Colorado School of Medicine, Denver. He has been a volunteer faculty member with the university medical school since 1911. He had been professor of pediatrics and head of the department from 1930 until his retirement on October 1.

ILLINOIS

Chicago

The Christian Fenger Lecture.—The eleventh Christian Fenger Lecture of the Institute of Medicine and the Chicago Pathological Society will be delivered at the Palmer House on Monday evening, January 13, by Dr. Robert A. Moore, Mallinckrodt professor of pathology and acting dean, Washington University School of Medicine, St. Louis, on "Interpretative Morphology."

Personal.—Dr. Fred L. Adair, emeritus professor of obstetrics and gynecology, University of Chicago, and formerly chief, medical staff, Chicago Lying-in Hospital, has received a grant-in-aid from the U. S. Department of State to enable him to serve as visiting lecturer in obstetrics in Argentina. While in Argentina Dr. Adair will lecture at the universities in Buenos Aires, Cordoba, Santa Fe and La Plata. He has been invited by the Society of Obstetrics and Gynecology of Argentina as a special delegate to the sixth Argentina Congress of Obstetrics and Gynecology.

Special Session on Chronic Illness.—On December 3 the Central Service for the Chronically Ill of the Institute of Medicine of Chicago devoted a special session to a discussion on "What Chicago Is Doing About Chronic Illness." The morning session was devoted to the prevention and control of chronic diseases and the afternoon session to long term care of chronically ill patients. Among the speakers were:

Mr. Leo M. Lyons, director, St. Luke's Hospital, Résumé of the Problems of Chronic Illness.

Dr. Andrew C. Ivy, Chicago, vice president, Chicago Professional Colleges University of Illinois, Chronic Diseases—Research and Medical Education in Relation to Prevention and Control.

Miss Edna S. Newman, director, Cook County School of Nursing, Education of Allied Professional Personnel for the Prevention and Control of the Chronic Diseases and the Care of People Disabled by Them.

Dr. John A. Rogers, executive director, Illinois division, American Cancer Society, Health Education and Community Agencies in Prevention and Control of Particular Diseases.

Dr. Carl Peterson, Chicago, Secretary, Council on Industrial Health, American Medical Association, Rehabilitation of Chronically Ill and Handicapped People.

Mr. Samuel A. Goldsmith, director, Jewish Charities of Chicago, Facilities and Services Needed for Care of Long-Term Patients.

Mr. Frank T. Loomis, executive director, Chicago Community Trust, Financial Aspects of Developing New Facilities.

Mr. Raymond M. Hilliard, public aid director, Illinois Public Aid Commission, Meeting the Costs of Care for Financially Dependent Patients.

Miss Mary E. Westphal, director, Visiting Nurse Association of Chicago, Care of Patients in Their Homes.

Dr. Roger W. De Busk, Evanston, president, Chicago Hospital Council; Rev. A. J. Munsterman, superintendent, Bensenville Home Society, Bensenville, Ill., and Miss Kathleen Cronin, superintendent, White Haven Acres, Glenview, Ill., Development of New Community Facilities for Care of Long-Term Patients.

Miss Edna Nicholson, director, Central Service for the Chronically Ill, The Role of the Central Service for the Chronically Ill.

New Wing for Research and Educational Hospitals.—Construction of a thirteen story wing to the Research and Educational Hospitals, University of Illinois College of Medicine, will begin about March 1. Of the total cost of the addition, $6,300,000, $2,200,000 is available from funds appropriated for the current (1945-1947) biennium. An additional sum of $4,100,000 is included in the university's total budget request for the 1947-1949 biennium for construction on the Chicago Professional College campus. Hospital bed capacity will be increased from 503 to 723 by the addition. At present the university's hospital beds total 227 in the general hospital, 120 in the Illinois Surgical Institute for Children (university orthopedic department) and 156 in the Illinois Neuropsychiatric Institute, which is owned by the department of public welfare but staffed and operated by the university. The thirteen story addition will connect with the present hospital at six levels on the north side and with the one story physical environment addition at one level on the west side. All three will be joined through an extension of the present tunnel system. Department clinical offices, research laboratories, x-ray and other adjunct services and operating rooms will be located on the second through the fifth floors. Floors 6 through 13 will contain hospital beds. Air conditioning will be installed in one of the hospital bed floors designed for 25 patients. The purpose is to provide special research and therapy under controlled temperatures. Operating rooms, delivery rooms and nurseries will also be air conditioned, and all floors will be so constructed that air conditioning may be installed later. The addition will be located on the west side of Wood Street between Polk and Taylor streets between the present hospital and the Illinois Neuropsychiatric Institute.

INDIANA

State Medical Election.—Dr. Cleon A. Nafe, Indianapolis, was chosen president-elect of the Indiana State Medical Association at its recent annual meeting and Dr. Floyd T. Romberger, LaFayette, will take office as president of the association January 1, succeeding Dr. Jesse E. Ferrell, Fortville. Dr. Arthur F. Weyerbacker, Indianapolis, is treasurer for another term. Named as delegates to the American Medical Association were Drs. Homer G. Hamer, Indianapolis, and Alfred S. Giordano, South Bend. French Lick was selected as the site for the 1947 convention.

Grant for Research in Gangrene.—Indiana University School of Medicine has received a grant of $15,000 from the National Institute of Health, U. S. Public Health Service, Bethesda, Md., to study the organisms concerned in the cause of gas gangrene of man and certain animals, according to the Indianapolis *News*, November 8. Leland S. McClung, Ph.D., Bloomington, associate professor of bacteriology, will be in charge of the program, and certain parts of the work will be done in cooperation with Harry G. Day, Sc.D., Bloomington, associate professor of chemistry.

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MARYLAND

Lecture Named for Julius Friedenwald.—On November 14 Dr. George B. Eusterman, Mayo Clinic, Rochester, Minn., gave the first annual Dr. Julius Friedenwald Memorial Lecture at the University of Maryland School of Medicine, Baltimore. His subject was "Newer Phases of Gastroduodenal Ulcer." The Friedenwald Lecture was established at the University of Maryland School of Medicine in Baltimore in 1941, following the death of Dr. Friedenwald, professor emeritus of gastroenterology at the Maryland medical school.

Institute for Mental Disorders.—Dr. Robert V. Seliger, Baltimore, has been named medical director of the newly organized Neuropsychiatric Institute of Baltimore, with headquarters at 2030 Park Avenue, Baltimore 17. The institute is a private outpatient arrangement for the investigation, understanding and treatment of nervous, mental, emotional and personality illnesses. In addition to the usual investigative and treatment technics, the institute is equipped with an electroencephalographic laboratory and has trained personnel to administer the various practical clinical psychologic test technics. Electric shock therapy is available for carefully selected patients. While the institute itself does not provide hospitalization, facilities are available to arrange for the care of patients requiring partial, semi or complete protective environment.

MICHIGAN

Changes in Health Personnel.—Dr. William B. Wild, Mansfield, Ohio, has been named director of the Barry County Health Department, filling the vacancy that occurred when Dr. John K. Altland, Hastings, resigned to become director of local health services of the Michigan State Department of Health, Lansing.

Dr. Cummings Goes to Ireland.—Dr. George D. Cummings, director of laboratories, Michigan State Department of Health, Lansing, was to leave November 9 for Dublin to direct an Irish Free State campaign against epidemic diarrhea in newborn infants, newspapers reported. Specimens requiring analysis will be flown from Ireland to Michigan, permitting examination in the Lansing laboratories twenty hours after the specimens are collected.

NEW YORK

Louise Beamis Resigns.—Dr. Louise W. Beamis has resigned as secretary of the Medical Society of the County of Erie, effective January 1, owing to illness of a member of her family. Dr. Beamis had held the secretaryship since 1929.

Buffalo Cancer Center.—Plans to establish a cancer center in Buffalo and the award of nineteen fellowships and grants totaling $135,455 for cancer research were announced November 6 by John Pennington, president of the state division of the American Cancer Society. The cancer center is to be used as a directional clinic to aid in early detection and arrest of the disease but will not be used for research or treatment. The fellowships and grants went to different hospitals, universities and other groups for work by specified individuals.

New York City

The Third Harvey Lecture.—Dr. Charles B. Huggins, professor of surgery (urology), University of Chicago School of Medicine, will deliver the third Harvey Society Lecture in the current series at the New York Academy of Medicine, December 19. His subject will be "The Prostatic Secretion."

Perkin Medal Goes to Robert Williams.—Robert R. Williams, D.Sc., director of research of the Research Corporation of New York, has won the 1946 Perkin Medal of the American section of the Society of Chemical Industry, according to the New York *Times*, November 25. The medal will be presented January 10.

Public Exhibit on Anesthesia.—Commemorating the hundredth anniversary of the discovery of ether, New York University College of Medicine opened to the public November 13 an exhibit on anesthesia in the library of the college at 477 First Avenue. Old and rare items connected with the history of anesthesia were on display until November 27.

New Professor of Surgery at Columbia.—Dr. John S. Lockwood, since 1924 chief of the division of surgery, committee on medical research of the Office of Scientific Research and Development, has been appointed professor of surgery at Columbia University College of Physicians and Surgeons. Dr. Lockwood will also serve as attending physician at the Presbyterian Hospital. Dr. Lockwood, who graduated at Harvard Medical School, Boston, in 1931, has for the past two years been associate professor of surgery at Yale University School of Medicine, New Haven, Conn.

SOUTH CAROLINA

Changes in Health Officers.—Dr. Charles I. Goodwin, Holly Hill, was appointed to succeed the late Dr. Grover C. Bolin as director of the Orangeburg and Calhoun County Health Departments, September 1. Dr. Caroline H. Callison, Chatham, has been granted a leave of absence as director of the Greenwood and McCormick County Health Departments to take a course in public health at Columbia University. During her absence Dr. Maulden J. Boggs Jr., health officer of Abbeville, will be in charge of the Greenwood and McCormick health units.

TEXAS

Postgraduate Assembly.—The postgraduate medical assembly of South Texas was held in Houston, December 3-5. Included among the speakers were:

Dr. Eugene F. Traub, New York, Dermatology.
Dr. Henry L. Bockus, Philadelphia, Gastroenterology.
Dr. Deryl Hart, Durham, N. C., Surgery.
Dr. Richard W. TeLinde, Baltimore, Gynecology.
Dr. Guy A. Caldwell, New Orleans, Orthopedics.
Dr. Lowrain E. McCrea, Philadelphia, Urology.
Dr. Paul H. Holinger, Chicago, Laryngology.
Dr. Frederick H. Falls, Chicago, Obstetrics and Gynecology.
Dr. James L. Wilson, Ann Arbor, Mich., Pediatrics.
Dr. Wendell L. Hughes, Hempstead, N. Y., Ophthalmology.
Dr. Fletcher D. Woodward, Charlottesville, Va., Otolaryngology.
Dr. Sidney A. Portis, Chicago, Medicine.
Dr. Edwin Hayden, Boston, Surgery.
Dr. Thomas D. Allen, Chicago, Ophthalmology.

University News.—Dr. George M. Decherd Jr., Galveston, has been appointed director of the student health service of the University of Texas at the Austin campus. He is relinquishing his positions at the medical branch at Galveston as director of the heart station and as director of the postgraduate training program but is retaining his title as professor of medicine. Dr. Truman G. Blocker Jr., Galveston, professor of surgery, has been appointed director of the postgraduate training program at Galveston.——Dr. Robert W. Davis, formerly associated with the department of psychiatry of the University of Colorado School of Medicine, Denver, has been appointed associate professor of neuropsychiatry at the University of Texas Medical Branch, Galveston, and assistant director of the Galveston State Psychopathic Hospital. Dr. Davis graduated at the University of Michigan Medical School, Ann Arbor, and received special training in psychiatry at the University of Colorado School of Medicine.

VIRGINIA

Division Heads Named.—Dr. J. C. Neale Jr., Norfolk, assistant director of the bureau of local health services, Virginia State Department of Public Health, has been named director and Dr. Peyton M. Chichester, Richmond, also an assistant director, has been chosen acting director of the bureau of tuberculosis outpatient service and crippled children's service. The Richmond *Times-Dispatch* reported on October 26 that both appointments were effective immediately. Dr. Jack B. Porterfield, who recently resigned as health officer of Richmond, effective November 15, will return to the state board of health as an assistant director in the bureau of local health services. He has been succeeded in the Richmond position by Dr. Charles Howe Eller, Baltimore.

WEST VIRGINIA

Personal.—Dr. Andrew E. Amick of Lewisburg has been named by Dr. Newman H. Dyer, state health commissioner, as district health officer and pediatric consultant for district number 2, composed of Greenbrier, Pocahontas and Monroe counties. Headquarters will be set up at Lewisburg. With the announcement of the appointment of Dr. Amick the commissioner said that the state health department is now working out details for a branch laboratory which, it is hoped, can be established and operated at Lewisburg under the supervision of Dr. Amick. Plans are still in the formative stage, but it is expected that the laboratory can be opened shortly after the first of the year. There has been a vacancy in the office of district health officer for district number 2 since 1944, when Dr. Herbert Duncan resigned to accept a residency in eye, ear, nose and throat at the Nashville General Hospital in Nashville.

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——Dr. Charles Taylor, Huntington, has been reappointed superintendent of the Huntington State Hospital, a position he has held since 1933.——Dr. Harry F. Coffman, Keyser, has been named by the Public Health Council as part time health officer for Mineral County.

WISCONSIN

The Loevenhart Memorial Lecture.—Dr. Walter C. Alvarez, Rochester, Minn., delivered the Dr. Arthur S. Loevenhart Memorial Lecture, December 5, at the University of Wisconsin Medical School, Madison, under the auspices of the Phi Delta Epsilon Medical Fraternity. Dr. Alvarez's subject was "Headache."

GENERAL

Dr. Foote Joins Society for Prevention of Blindness.—Dr. Franklin M. Foote, recently discharged from service in the Army of the United States, has been appointed medical director of the National Society for the Prevention of Blindness, 1790 Broadway, New York 19. Dr. Foote retains his position as assistant professor of public health and preventive medicine at Cornell University Medical College.

New Journal on Postgraduate Medicine.—The official publication of the Inter-State Postgraduate Medical Association of North America will be published beginning January 1947, announces Dr. Arthur G. Sullivan, managing director of the Interstate Postgraduate Medical Association of North America. The business manager, Paul K. Whipple, who is located at 515 Essex Building, Minneapolis, is already receiving space commitments for the first issue. The subscription price is $8 per year.

Vitamin Foundation Approves Grants.—The National Vitamin Foundation at its first dinner meeting at the Waldorf-Astoria Hotel, November 15, announced that it had approved six grants-in-aid, totaling $23,300. The new grants include:

Willard A. Krehl, Yale University School of Medicine, $2,000, alteration of vitamin requirements induced by natural foodstuffs.

Barnett Sure, Ph.D., professor of agricultural chemistry, University of Arkansas, Fayetteville, $3,000, influence of the various components of the vitamin B complex on protein utilization.

Dr. James J. Smith, assistant in medicine, New York University College of Medicine, $1,500, determinations of biochemical base lines for studies of vitamin-hormone interrelationships.

Dr. William J. Darby, assistant professor of biochemistry and medicine, and Dr. Edgar Jones, associate professor of clinical medicine, Vanderbilt University School of Medicine, Nashville, $3,800, the hemopoietic activity and other physiologic properties of the vitamin M group of substances.

Dr. Tom D. Spies, associate professor of medicine, University of Cincinnati College of Medicine, $5,000, relation of nutrients to white blood cell formation.

Max K. Horwitt, Ph.D., Elgin State Hospital, Elgin, Ill., $8,000, study of riboflavin in human nutrition.

New Psychiatric Foundation.—The organization of the Psychiatric Foundation has been announced. The group is being developed by the American Psychiatric Association and sponsored by the American Neurological Society. Dr. Leo H. Bartemeier, Detroit, secretary of the American Psychiatric Association, is in charge of the group designated by the association to assume responsibility for the new foundation during the organization period. Objectives: education of members of the psychiatric team in the psychiatric field; psychiatric research; medical legislation; child psychiatry; education of the public, and policy as to fund raising. In addition to Dr. Bartemeier the organization committee includes Drs. Edward A. Strecker, Philadelphia; Frederick Parsons, New York; Karl M. Bowman, San Francisco; Arthur H. Ruggles, Providence, R. I.; Winfred Overholser, Washington, D. C.; Harry C. Solomon, Boston; Gregory Zilboorg, New York City; C. Charles Burlingame, Hartford, Conn.; Mesrop A. Tarumianz, Farnhurst, Del., and Mr. D. Walker Wear, New York. Austin M. Davies is executive director, and headquarters are in room 924, 9 Rockefeller Plaza, New York.

Directory of Convalescent Homes.—The Committee on Public Health Relations of the New York Academy of Medicine is preparing a new edition of the "Directory of Convalescent Homes in the United States," to be published by the Sturgis Fund of the Winifred Masterson Burke Relief Foundation of White Plains, New York. The last issue of this directory was published by the Sturgis Fund in 1931 under the auspices of the Committee on Convalescent Care of the American Conference on Hospital Service and has long been out of print. Early in January a questionnaire will be distributed to all recognized convalescent homes maintained by municipalities, counties or voluntary bodies. The information sought deals with the physical plant, the staff, the requirements for admission, the type of patients, therapy and such other matters as will make the directory a dependable guide for physicians who wish to refer their patients to institutions for convalescence. The questionnaire is so devised that it can be filled out with a minimum of effort. Convalescent homes that do not receive a questionnaire are urged to request one by writing to E. H. L. Corwin, Executive Secretary, Committee on Public Health Relations, New York Academy of Medicine, 2 East 103d Street, New York 29.

Borden Award in Nutrition.—The American Institute of Nutrition will present the Borden Award in recognition of distinctive research by investigators in the United States and Canada which has emphasized the nutritive significance of the components of milk or of dairy products. The award will be made primarily for the publication of specific papers, but the judges may recommend that it be given for important contributions over an extended period of time. The award may be divided between two or more investigators. Employees of the Borden Company are not eligible for this honor. The formal presentation will be made at the annual meeting of the institute in Chicago, May 18-22, 1947. To be considered for the award, nominations must be in the hands of the chairman of the nominating committee by Jan. 15, 1947. The nominations should be accompanied by such data relative to the nominee and his research as will facilitate consideration for the award. The chairman is Genevieve Stearns, Ph.D., State University of Iowa College of Medicine, Iowa City.

Research Council to Study Pollen Distribution.—A research council to study pollen distribution throughout the nation in an effort to help present sufferers from hay fever is being set up by the American Academy of Allergy, the New York *Times* reported November 26. The plan calls for the formation of three major divisions to deal with aeroallergens, foods and drugs and pharmaceuticals. The work of the council will be modeled after the Committee on Aerobiology of the National Research Council. Members of the council are to be appointed by the executive committee of the academy in December. The first subject to be studied will be air borne substances causing allergies. Subcommittees will deal with four major divisions of allergens—pollens, molds, dust and miscellaneous allergens, and air processing. Among the projects the subcommittees will prepare will be a daily pollen count map to be made in cooperation with the United States Weather Bureau. The map will be offered to newspapers for publication. The academy has allocated $1,000 for initial administrative expenses of the new group. Additional financing will be sought from foundations and private contributors.

Francis Amory Prize.—In compliance with the terms of a gift under the will of the late Francis Amory, Beverly, Mass., the American Academy of Arts and Sciences offers a substantial prize for meritorious work addressed to the alleviation or cure of diseases affecting human reproductive organs. The gift provides a fund the income of which may be awarded at seven year intervals "as a prize and gold medal, or other token of honor or merit," to any individual or individuals for work of "extraordinary or exceptional merit" in this field. In case there has appeared work of a quality to warrant it, the next award will be made in 1947. Awards will be made for what in the judgment of the Committee on the Amory Fund appears to be the most distinctive contribution or contributions in the field as outlined and as based on published work and recognized accomplishment for the current seven year period. No formal applications and no essays or treatises from individuals are solicited, but suggestions will be welcome from any appropriate source that will be of aid to the committee in making a wise selection. Recommendations may be addressed to Secretary, Amory Fund Committee, American Academy of Arts and Sciences, 28 Newbury Street, Boston.

Marriages

JOHN KELLAM LINGO, Pungateague, Va., to Miss Hilda Sinclaire Jervis of Marshall, N. C., in New York August 14.

JOHN J. ARCHINARD JR., New Orleans, to Miss Zelma Claudia Weaner of Shreveport, La., April 13.

ROBERT B. ROBERTSON, Presque Isle, Maine, to Mrs. Ellen Pegues Godfrey in New York recently.

AUGUST H. KRAMM, Washington, D. C., to Miss Margaret Cotter in Rockville, Md., recently.

BURTON SINCLAIR WILT to Miss Frances Dowling, both of Wing Point, Wash., September 10.

FRANK COLE, Duluth, Minn., to Miss Doris Cohen of Superior, Wis., August 31.

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Deaths

Alice Stone Woolley ✠ Poughkeepsie, N. Y.; born in Yankton, S. D., Sept. 12, 1882; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1930; interned at the Gallinger Municipal Hospital in Washington, D. C., where she was resident physician at the Children's Hospital; past president and chairman of the international relations committee of the American Medical Women's Association; past president and vice president of the Women's Medical Society of New York State; decorated by the French government in recognition of her two years of military service overseas during World War I; appointed by Governor Dewey to the board of visitors of the New York State Training School for Girls, Hudson; served as director of the Dutchess County Health Association, a member of the council of the Dutchess County Girl Scouts and the board of directors of the Dutchess County chapter of the American Red Cross; director of physical education at the local Y. W. C. A. from 1908 to 1925; member of the courtesy staffs of the Northern Dutchess Health Service Center, Rhinebeck, St. Francis and Vassar Brothers hospitals; member of the board and vice president of the Bowne Memorial Hospital; on the board of the Samuel and Nettie Bowne Hospital; medical consultant for Bard College, Annandale-on-Hudson; associate editor of the *Journal of the American Medical Women's Association;* died in the Doctors Hospital, New York, November 16, aged 64, of coronary thrombosis and bronchopneumonia.

Marion Hague Rea ✠ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1915; born in Denver July 21, 1885; served an internship at the Philadelphia General Hospital (Blockley Hospital) 1915-1916 and as assistant physician at the Boston Psychopathic Hospital, 1916-1917; returned to Philadelphia to become chief resident physician of the Hospital of the Woman's Medical College of Pennsylvania, in which capacity she served for one year and later assistant and associate in medicine, serving from 1917 to 1923; resident physician at Bryn Mawr (Pa.) College from 1918 to 1920 and in 1923 and 1924; assistant visiting physician to the Philadelphia General Hospital from 1917 to her death; served as instructor in medicine at the University of Pennsylvania School of Medicine since 1918; medical director in the department of physical education for women at the University of Pennsylvania from 1921 to 1935; since 1922 chief in medicine at the Woman's Hospital; died suddenly November 1, aged 61, of myocarditis.

Irving Samuel Haynes ✠ Plattsburg, N. Y.; born in Saranac, N. Y., Aug. 29, 1861; University of the City of New York Medical Department, New York, 1887; professor of clinical surgery emeritus at Cornell University Medical College, New York; fellow of the American College of Surgeons; served as medical superintendent of the Physicians Hospital, where he has been a member of the board of directors since 1944; consulting surgeon to the Reconstruction and Harlem hospitals in New York and the Glens Falls (N. Y.) Hospital; author of "Practical Guide for Beginners to the Dissection of the Human Body" and "Manual of Anatomy"; received the doctor of science degree from Wesleyan University in 1915; died October 9, aged 85.

William Schaeffer Bertolet ✠ Reading, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; first president of the Diplomates' Association of Berks County Physicians; served as chairman of the Berks County Medical Advisory Board during World War I; held honorary degrees of doctor of science from Albright College and Franklin and Marshall College; medical director of the Reading Hospital, where he served for many years in various capacities and where he died October 9, aged 71, of heart disease.

Charles James Roach, Zanesville, Ohio; Ohio State University College of Medicine, Columbus, 1917; member of the American Medical Association; won many decorations for outstanding and meritorious service during World War I; company physician for the American Rolling Mill Company, Firestone Tire and Rubber Company and Zanesville Aerie of Eagles, receiving a congressional certificate of merit for his services in this capacity during World War II; served as chief of the staff of the Good Samaritan Hospital, where he died September 21, aged 56, of leukemia.

Ernest E. Billings, Kingston, N. Y.; University of the City of New York Medical Department, New York, 1884; member of the American Medical Association; on the staffs of the Benedictine and Kingston hospitals; died October 4, aged 87, of chronic myocarditis.

George Houghton Bodley ✠ New Britain, Conn.; Yale University School of Medicine, New Haven, 1907; served on the staff of the New Britain General Hospital; died July 12, aged 66, of pneumonia.

Herschel Baker Bray, Wrightsville, Ga.; Emory University School of Medicine, Atlanta, 1922; member of the American Medical Association; interned at the Grady Memorial Hospital in Atlanta; served during World War I; died July 2, aged 51.

Hiester Bucher ✠ Reading, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; served on the staff of the Reading Hospital; died August 1, aged 74, of coronary occlusion.

William Roy Cain, Tyler, Texas; University of Texas School of Medicine, Galveston, 1909; member of the American Medical Association; served in France during World War I, for which he received the Purple Heart and was cited for meritorious service by both French and United States commanders; for two and half years ophthalmologist with the U. S. Army induction station at Tyler; for many years city health officer; found dead August 11, aged 59, of coronary occlusion.

Enoch J. Cook, Monahans, Texas (licensed in Texas under the Act of 1907); for two years served with the Selective Service Board; died August 7, aged 69, of cerebral hemorrhage.

Linus Reed Cranmer ✠ Steubenville, Ohio; University of Michigan Medical School, Ann Arbor, 1915; interned at the Lakeside Hospital in Cleveland; resident physician for the Wheeling Steel Company and the Pennsylvania Railroad; on the staffs of the Ohio Valley and Gill Memorial hospitals; died September 17, aged 56, of coronary thrombosis.

Carl Frederick Dick, St. Louis; University of Nashville (Tenn.) Medical Department, 1901; founder of the Dick-X-Ray Company; died in the Barnes Hospital October 20, aged 68, of coronary disease.

John Henry Donovan, Lowell, Mass.; College of Physicians and Surgeons, Boston, 1905; died September 10, aged 65, of cerebral hemorrhage.

Lee Bennett Gardner, Geneva, N. Y.; Eclectic Medical College, Cincinnati, 1899; member of the American Medical Association; on the staff of the Geneva General Hospital, where he died September 1, aged 73, of ruptured gastric ulcer.

Robert Willis Hatch, Indianapolis; University of Minnesota Medical School, Minneapolis, 1932; diplomate of the National Board of Medical Examiners; died in the City Hospital September 8, aged 40, of portal cirrhosis.

Robert G. Henderson, Falls City, Neb.; Kansas City Medical College, 1900; member of the American Medical Association; affiliated with Our Lady of Perpetual Help Hospital; died September 25, aged 74, of coronary thrombosis.

Henry Francis Kinsman ✠ Hamlet, N. C.; University of Vermont College of Medicine, Burlington, 1894; died in the Memorial Hospital, Charlotte, August 24, aged 74, of pneumonia.

Charles E. Mays, San Angelo, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1885; honorary member of the State Medical Association of Texas; past president of the Tom Green County Medical Society; served on the staffs of St. John's Hospital and the Shannon West Texas Memorial Hospital, where he died June 20, aged 84, of pneumonia.

Thomas J. Pennebaker, Cotton Plant, Miss. (licensed in Mississippi in 1891); died September 12, aged 87, of arteriosclerosis.

Henry Ruffu, Atlantic City, N. J.; Chicago Medical School, 1928; died in the Atlantic City Hospital September 23, aged 48.

Franklin Wesley Sells ✠ Osceola, Iowa; Drake University Medical Department, Des Moines, 1896; died September 27, aged 73, of cerebral hemorrhage.

Anthony Claudius Thiolliere, North Little Rock, Ark.; Université de Lyon Faculté de Médecine et de Pharmacie, France, 1894; Dallas Medical College, 1903; member of the American Medical Association; a captain in the medical corps of the U. S. Army during World War I; died September 2, aged 73, of cerebral hemorrhage and hypertension.

Lawrence Patrick Tully, Iron River, Michigan; Marquette University School of Medicine, Milwaukee, 1923; served during World War I; died in the Veterans Administration Hospital in Milwaukee, July 26, aged 49, of pulmonary tuberculosis.

William Morris Watkins, Louisville, Ky.; Kentucky University Medical Department, Louisville, 1904; served during World War I; died in St. Anthony's Hospital September 16, aged 73, of pneumonia complicating cerebral hemorrhage.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 16, 1946.

The British Medical Association and the National Health Insurance Act

The national health service bill has become law, but the opposition of the British Medical Association has only reached its climax. The association has posted voting forms to all doctors on the medical register asking them to answer Yes or No to the question "Do you desire the negotiating committee to enter into discussions with the minister on the regulations authorized by the National Health Service Act?" They are asked to return the form by November 30 or as soon as possible if in practice oversea. They are asked to state the number of years since qualification and the branch in which they practice. On the plebiscite form they are informed that the time has now come for a crucial decision of the profession. The act authorizes the minister of health now to proceed to regulations dealing with a wide variety of subjects, including the mode of and amount of professional remuneration, the terms and conditions of service generally and the composition of the regional hospital boards. The immediate issue which confronts the profession is whether it will or will not enter into discussions with the minister on the subject matter of those regulations. This issue the association places before the profession as a whole to determine by plebiscite. Those who hold that, notwithstanding the divergence between the principles of the profession and the provisions of the act, discussions should be entered into will answer Yes to the appended question. A decision to enter into discussion does not involve a decision to enter the service. Those who hold that, because of the wide divergence between the principles of the profession and the provisions of the act, the profession should decline to accept service under the scheme, whatever the conditions, will not authorize discussions and will answer No. If a sufficient number give a negative answer, the association will take the necessary action and prepare for the inevitable conflict. Implicit in such a vote is an undertaking, if so advised by the association, not to enter the new service.

The plebiscite form is accompanied by a letter from Dr. Hill, the secretary of the British Medical Association, which summarizes the more important issues on which the Representative Body differed with the government scheme: 1. There should be no control over doctors with regard to the area in which they wish to practice. 2. The transference of hospitals to state ownership was not approved. 3. It is essential to the freedom of the patient and of the profession that doctors should retain the good will of their practices. 4. Remuneration should be by capitation payments. 5. Any doctor, whether a specialist or a general practitioner, must have all the facilities for treating patients that are now held. The plebiscite form is also accompanied by a summary of the act and a report of the negotiating committee of the profession showing the main divergencies of the act from the views expressed by the organized bodies of the profession.

Paludrine in Malaria

At the Royal Society of Tropical Medicine and Hygiene, Professor Hamilton Fairley described remarkable results from the treatment of malaria by the new drug paludrine in the Australian army campaigning in the southwestern Pacific. The medical research unit of the Australian army experimentally infected with malaria 850 healthy volunteers. More than 200 were treated with paludrine, a biguanide derivative, while many hundreds of troops with relapsing benign tertian malaria were treated with the drug under controlled conditions. While taking 100 mg. of paludrine daily for three weeks after being infected with Plasmodium falciparum by infected mosquitoes, volunteers did not develop any symptoms of malaria and parasites were never demonstrated in their blood either microscopically or by subinoculation into fresh volunteers. Thus the drug acted as a causal prophylactic in falciparum infections. After infection with Plasmodium vivax a similar result was obtained. But on ceasing to take the paludrine all those infected subsequently developed delayed attacks of overt vivax malaria. Thus paludrine acted only as a partial prophylactic against benign tertian infections. Volunteers received as many as 130 P. falciparum and 120 P. vivax infections while taking 100 mg. of paludrine daily. During this time they were subjected to severe stresses and strains, including long marches in a tropical climate, chilling by exposure in a freezing chamber and injections of epinephrine and insulin. The daily dose of paludrine was continued for four weeks after the last exposure to infection, which covered a period of two months. Throughout the period of three months no symptoms of malaria were observed and parasites were never demonstrated in the blood. Some twenty-four to thirty-three days after the last dose of paludrine overt vivax malaria developed, but never falciparum malaria.

The practical conclusion from these and other experiments is that paludrine 100 mg. twice weekly will entirely prevent falciparum infection and will suppress vivax malaria throughout the period of administration. The significant quality of paludrine as a schizonticide is the smallness of the dose required to resolve a clinical attack of malaria. A single tablet of 100 mg. will cause disappearance of symptoms and of parasites from the blood, but radical cure is not to be expected from this dose. An entirely new field in the chemotherapeutic control of malaria is opened up by paludrine.

BRAZIL

(From Our Regular Correspondent)

São Paulo, Nov. 22, 1946.

Etiology and Treatment of Arterial Hypertension

Dr. Francisco Xavier de Pinto Lima and Dr. José Engelberg call attention to the factors which assume a role in essential hypertension as well as to the modern conception of that condition such as the phenomena of humoral factors with a predominantly renal origin. There are in the circulation humoral complexes which are formed or stored in different organs of hypertensive and hypotensive patients.

Dr. Lima and Dr. Engelberg present the details of organotherapy in hypertension. To strengthen their point of view they present graphs made in experiments on animals.

Hodgkin's Disease

Based on previous studies and his own observations, Professor Alexandre Donati states that Hodgkin's disease is an infectious reticuloendotheliosis and the infectious agent is the virus discovered by Gordon. The allergic state which develops in the patients is used by Dr. Donati for an intradermal test with diagnostic finality. Dr. Donati points out the advantages of vaccination therapy over roentgen therapy.

Hospitals in Brazil in 1943

In 1943 Brazil had 1,575 hospitals with a capacity of 117,304 beds. The states that have more hospitals are São Paulo with 377, Minas Geraes with 259, Rio Grande do Sul with 250, Distrito Federal with 107, the state of Rio de Janeiro with 92, Paraná with 91, Santa Catarina with 72, Baía with 66 and Pernambuco with 42; the other states have less than 30 hospitals.

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POSTGRADUATE CONTINUATION COURSES FOR VETERAN AND CIVILIAN PHYSICIANS

Compiled by the Council on Medical Education and Hospitals for Period Jan. 1, 1947 to July 15, 1947

Medical schools, hospitals, state medical societies and other medical educational institutions and organizations are providing the Council with a growing body of information on courses designed primarily to meet the needs of returning medical officers. These have been incorporated into the lists on these pages. They are not specifically designated for veterans, since most if not all of them may also be open to interested civilian physicians. Furthermore, all courses listed which were not designed primarily for physician veterans are also open to qualified returning medical officers.

Note that each course is listed only once, without cross indexing, so that in some instances a prospective student should look under more than one heading for a desired course.

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	ALLERGY		
University of Southern California, Division of Graduate Medicine, 3551 University Avenue, Los Angeles At: Los Angeles County Hospital	Allergy, Course No. 737	4 evening lectures, 1 evening weekly, April 2, 1947	$ 25 [1]
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Allergy	1 month, full time, 1st of every month except January	200
	Personal Course in Allergy and Related Conditions	To be announced; 10 weeks, 1 day each week	80
University of Illinois College of Medicine, 1853 West Polk Street, Chicago	Allergy	Jan. 6, 1947-Jan.5, 1948, full time	300 res. 600 non-res.
The American College of Allergists, Inc., 401 La Salle Medical Building, Minneapolis 2 At: University of Kansas School of Medicine, Kansas City, Kan.	Mississippi Valley Sectional Instructional Course in Allergy	May 5-7, 1947	35
Maine Medical Association, 177c Main Street, Waterville, Me. At: Boston	Allergy	Arranged, 1-2 weeks	Arranged [2]
Tufts Medical School Postgraduate Division, 30 Bennet Street, Boston At: Boston Dispensary and Pratt Diagnostic Hospital, Boston	Allergy	May 19-23, 1947, 5 days, full time	40
University of Michigan Medical School, Department of Postgraduate Medicine, 1313 East Ann Street, Ann Arbor, Mich.	Allergy	Spring, 1947, 1 week	30
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2	Allergy	April 14, 1947, 8 sessions, once a week, part time	20
Columbia University Faculty of Medicine, 630 West 168th Street, New York 32 At: Mount Sinai Hospital	Allergy PM 36 (Medicine)	March 10-22, 1947, 12 days, part time	20
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Allergy	Jan. 10-Feb. 28, 1947, 2 months, part time	25
	Allergy	April 7-25, 1947, 3 weeks, full time	200
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Allergy	Jan.-March, 1947, 2 months, once weekly	50
Graham-Thomas Clinic, 201 West Franklin Street, Richmond, Va.	Fellowship in Allergy	Jan. 1, 1947, 1 year, in selected cases 6 months	None
	ANATOMY		
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Surgical Anatomy on Cadaver and Clinical Program	Feb. 17, 1947, 2 weeks, full time	$150
	Surgical Anatomy on Cadaver and Clinical Program	March 17, 1947, 2 weeks, full time	150
	Surgical Anatomy on Cadaver and Clinical Program	April 14, 1947, 2 weeks, full time	150
	Surgical Anatomy on Cadaver and Clinical Program	May 12, 1947, 2 weeks, full time	150
	Surgical Anatomy on Cadaver and Clinical Program	June 9, 1947, 2 weeks, full time	150
	Surgical Anatomy on the Cadaver	To be announced 10 weeks, part time	125
University of Maryland School of Medicine, Lombard and Greene Street, Baltimore	Surgical Anatomy	15 weeks, Jan. 27-June 7, 1947	150
University of Michigan Medical School, 1313 East Ann Street, Ann Arbor, Mich.	Anatomy	March-June, 1947 15 days, full time	30
	Anatomy	Spring, 1947, 1 day a week	30
Creighton University School of Medicine, 306 North 14th Street, Omaha	Anatomy	Arranged, 3 months	None
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2	Anatomy	Jan. 6-April 18, 1947, 4 months, twice weekly	75

References will be found on page 946.

Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	ANATOMY—Continued		
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Anatomy of the Abdomen	Spring, 1947, 100 hours, arranged	150
	Applied Anatomy for the Anesthetist	Spring, 1947, 125 hours, arranged	275
	Applied Anatomy for the General Surgeon	Spring, 1947, 250 hours, arranged	375
	Applied Anatomy for the Otolaryngologist	Spring, 1947, 150 hours, arranged	275
	Anatomy for the Orthopedic Surgeon	Spring, 1947, 100 hours, arranged	150
	Anatomy of the Thorax	Spring, 1947, 100 hours, arranged	150
	Applied Anatomy of Urogenital System	Arranged, 130 hours, arranged	300
	Microscopic Anatomy—Histogenesis	Arranged, 20 weeks, half time	150
University of North Carolina School of Medicine, Chapel Hill, N. C.	Anatomy	Arranged	25
Duke University School of Medicine, Durham, N. C.	Anatomy	Arranged, 3 months or longer, full time	150 per qtr.
	ANESTHESIOLOGY		
George Washington University School of Medicine, 1335 H Street, N. W., Washington, D. C. At: School of Medicine and various hospitals	Intensive Refresher Course in Anesthesiology	Feb. 10-14, 1947, 1 week, full time	50
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Inhalation Anesthesia	First of every month, 1 month, full time	200
University of Minnesota Medical School, Minneapolis 14 At: Center for Continuation Study	Anesthesiology	To be announced, 3, 6, or 12 days	15 25 50
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Clinical Anesthesiology	Arranged, 3 months, full time	250
New York Polyclinic Medical School and Hospital, 341 West 50th Street, New York 19	Applied Anesthesia	Jan. 1947, 3 months	Not given
	Applied Anesthesia	April, 1947, 3 months	300
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Anesthesia [5]	Arranged, 2 weeks, full time	100
New York University College of Medicine, 477 First Avenue, New York At: Beth Israel Hospital	Anesthesiology	Jan. 6, 1947, 24 weeks, full time	400
Duke University School of Medicine, Durham, N. C.	Anesthesiology	Arranged, 3 months or longer, full time	150 per qtr.
University of Texas Medical Branch, 912 Avenue B, Galveston, Texas	Inhalation, Spinal Block, Intravenous Anesthesia	Arranged, 3-6 weeks	Not given
	ARTHRITIS		
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Arthritis and Allied Rheumatic Disorders	Jan. 7-Feb. 25, 1947, 2 months, part time	$ 45
	Arthritis and Allied Rheumatic Disorders	April 21-25, 1947, 5 days, full time	45
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2	Arthritis	April 14, 1947, 8 sessions, once a week, part time	20
New York University College of Medicine, 477 First Avenue, New York 16	Arthritis and Rheumatic Disorders	Spring, 1947, 6 weeks, part time	100
At: Bellevue Hospital	Arthritis and Rheumatic Disorders	Winter, 1947, 6 weeks, part time	100
	BACTERIOLOGY		
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Clinical Bacteriology and Serology	Jan. 2-31, 1947, 1 month, part time	$100
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Bacteriology	Arranged	100
New York University College of Medicine, 477 First Avenue, New York 16	Bacteriology	March 3, 1947, 16 weeks, part time	50 vets. 60 non-vets.
University of North Carolina School of Medicine, Chapel Hill, N. C.	Bacteriology and Immunology	Arranged	25
Duke University School of Medicine, Durham, N. C.	Bacteriology and Parasitology	Arranged, 3 months or longer, full time	150 per qtr.
	BASIC SCIENCES		
University of Southern California, Division of Graduate Medicine, 3551 University Avenue, Los Angeles 7 At: Los Angeles County Hospital	Basic Science Course No. 736	Jan. 3, 1947-Jan. 2, 1948, 1 year, part time	$200 per yr. 50 per qtr.
University of California Medical School Extension, San Francisco 22	Course in Basic Sciences	Summer, 1947	Not given [20]
	Review Course in the Basic Sciences (for preparation to specialty boards examinations)	June-Sept. 1947, 16 weeks, full time	See [3]
University of Illinois College of Medicine, 1853 West Polk Street, Chicago	Basic Medical Sciences	Jan. 1, 1947, 36 weeks, full time	600 [4]
Tufts Medical School Postgraduate Division, 30 Bennet Street, Boston, Mass. At: Pratt Diagnostic Hospital	Review of Basic Sciences	May-June, 1947, 8 weeks, full time	200 [1]
University of Minnesota Medical School, Minneapolis 14 At: Center for Continuation Study	Basic Sciences and Their Clinical Application	Jan. 6-March 20, 1947, 11 weeks, full time	20 per wk.
	Basic Sciences and Their Clinical Application	March 31-June 13, 1947, 11 weeks, full time	20 per wk.
Creighton University School of Medicine, 306 North 14th Street, Omaha	Clinical Basic Science Conference	Arranged, 3 months	None
Southwestern Medical College of Southwestern Medical Foundation, 2211 Oak Lawn, Dallas, Texas	Postgraduate Course in Basic Sciences	March 9-May 30, 1947, 12 weeks, full time	$300
University of Wisconsin Medical School, 418 North Randall Street, Madison 6, Wis.	Divisions of the Basic Sciences	Continuous	100 per mo.
	BIOCHEMISTRY		
New York University College of Medicine, 477 First Avenue, New York 16	Biochemistry	March 3, 1947, 16 weeks, part time	$75 non-vets. 65 vets.
University of North Carolina School of Medicine, Chapel Hill, N. C.	Biochemistry	Arranged	25
Duke University School of Medicine, Durham, N. C.	Biochemistry	Arranged, 3 months or longer	150 per qtr.

References will be found on page 946.

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
CARDIOVASCULAR DISEASE			
College of Medical Evangelists, 312 North Boyle Avenue, Los Angeles 33 At: White Memorial Hospital	Cardiology	Jan. 14, 1947, 12 weeks, 1 evening a week	35
American College of Physicians, 4200 Pine St., Philadelphia At: University of Southern California, Los Angeles	Cardiovascular Disease [5]	Feb. 3-7, 1947, 1 week	$ 20 mem. 40 non-mem.
George Washington University School of Medicine, 1335 H St., N. W., Washington, D. C.	Intensive Postgraduate Course in Cardiovascular Disease	Feb. 17-21, 1947, 1 week, full time	50
American College of Physicians, 4200 Pine St., Philadelphia At: Emory University School of Medicine, Atlanta, Ga.	Cardiovascular Disease [5]	March 31-April 5, 1947, 1 week	20 mem. 40 non-mem.
University of Georgia School of Medicine, University Place, Augusta, Ga.	Cardiology	Arranged, 2 weeks	50 res. 75 non-res.
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Course in Cardiovascular-Renal Diseases	Feb. 1947 (tentative), 10 weeks, 1 day each week	60
	Course in Cardiovascular-Renal Diseases	April 1947 (tentative), 10 weeks, 1 day each week	60
American College of Physicians, 4200 Pine St., Philadelphia At: Northwestern University Medical School, Chicago	Cardiovascular Disease [5]	April 21-26, 1947, 1 week	20 mem. 40 non-mem.
Tulane University of Louisiana School of Medicine, 1430 Tulane Avenue, New Orleans 13	Cardiovascular System Diseases	Feb. 3-8, 1947, 5½ days, full time	25
Maine Medical Association, 177c Main St., Waterville, Me. At: Boston	Cardiology	Arranged, 1-2 weeks	None [1]
Tufts Medical School Postgraduate Division, 30 Bennet Street, Boston, Mass. At: Pratt Diagnostic Hospital	Cardiology	May 12-16, 1947, 5 days, full time	40
University of Michigan Medical School, 1313 East Ann Street, Ann Arbor, Mich.	Diseases of the Heart	Spring, 1947, 5 days, full time	30
University of Buffalo Medical School, 24 High Street, Buffalo	Heart Disease (Seminar)	Feb. 1947, 3 days	Not given
Columbia University, 630 West 168th Street, New York 32 At: Montefiore Hospital At: Mount Sinai Hospital	Advanced Cardiology	Jan.-June, 1947, 5 months, part time	150
	Cardiovascular Disease	Feb. 3-March 8, 1947, 5 weeks, part time	75
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Cardiology	Jan. 6-Feb. 24, 1947, 2 months, part time	45
	Cardiology	May 5-29, 1947, 4 weeks, full time	125
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2	Clinical Cardiology	April 15, 1947, 8 sessions, once a week, part time	20
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Cardiology	April, 1947, 2 weeks, part time	150
New York Polyclinic Medical School and Hospital, 341 West 50th Street, New York 19	Diagnosis and Treatment of Diseases of the Heart	Arranged, 3 weeks, part time	75
New York University College of Medicine, 477 First Avenue, New York 16 At: Beth Israel Hospital	Cardiovascular Disease	Feb. 20, 1947, 12 weeks, part time	50
University of Oregon Medical School, West Marquam Hill Road, Portland 1, Ore.	Cardiology	Jan. 13-17, 1947, 5 days, full time	50
University of Wisconsin Medical School, 418 North Randall Street, Madison 6, Wis.	Observation Course in Cardiology	Jan. 1947, 5 days, full time	25
CHEMISTRY			
Duke University School of Medicine, Durham, N. C.	Seminars in Clinical Chemistry	Arranged, 10-12 weekly seminars	$150 per qtr.
	Practical and Theoretical Instruction in Clinical Chemistry	Arranged, 3 months, full time	150 per qtr.
CHEST DISEASES			
California Tuberculosis and Health Association, 45 Second Street, San Francisco At: Medical Schools in Los Angeles	Tuberculosis	Arranged, 3 days-2 weeks	None
University of Southern California Division of Graduate Medicine, 3551 University Avenue, Los Angeles At: Los Angeles County Hospital	Pulmonary Diseases, Course No. 740 (Lectures)	April 2, 1947, 12 weeks, 1 evening a week	$ 50 [1]
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Technic of Physical Examination and Diagnosis of Chest	To be announced, 8 weeks, part time, 1 day each week	80
Municipal Tuberculosis Sanitarium, 5601 North Pulaski Road, Chicago	Postgraduate Course in Tuberculosis	Jan.-July 15, 1947, daily	None
Tulane University of Louisiana School of Medicine, 1430 Tulane Avenue, New Orleans 13	Pulmonary Diseases	Jan. 27-Feb. 1, 1947, 5½ days	25
State Sanatorium, Sanatorium, Miss.	Chest Diseases	All year, continuously, 2 weeks	None
	Chest Diseases	Continuously, 6 months	None
Columbia University, 630 West 168th Street, New York 32 At: Columbia Presbyterian Medical Center	Recent Advances in the Treatment of Bronchial Asthma, Bronchiectasis and Pulmonary Emphysema	Jan. 27-Feb. 1, 1947, 6 days, full time	40
At: Montefiore Hospital	Medicine PM 63—Diseases of the Chest	Jan. 3-May 16, 1947, 19 weeks	60
At: Mount Sinai Hospital	Medicine PM 37—Diseases of the Chest	March 10-22, 1947, 12 days, part time	30
Columbia University—At: New York Post-Graduate Medical School, 303 East 20th Street, New York 3	Acute and Chronic Diseases of the Chest	Jan. 9-Feb. 27, 1947, 2 months part time	45
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Pulmonary Tuberculosis	June, 1947, 1 month	150
Wisconsin Anti-Tuberculosis Association, 324 East Wisconsin Avenue, Milwaukee At: Health Service Building, 1018 North Jefferson Street, Milwaukee	Essentials of Chest X-Ray Films and Their Interpretation	Between Jan. 1-July 1, 1947, 6 weeks, 2 hours a week	Not given
DERMATOLOGY AND SYPHILOLOGY			
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Lecture and Clinical Course in Dermatology	April 14, 1947, 2 weeks, full time	$100
	Lecture and Clinical Course in Dermatology	June 16, 1947, 2 weeks, full time	100
University of Illinois College of Medicine, 1853 West Polk Street, Chicago	Postgraduate Dermatology	Feb.-Nov., 1947, 9 months	500
University of Kansas School of Medicine, Kansas City, Kan. At: University of Kansas Hospitals	Internal Medicine and Dermatology	March 17-21, 1947, 5 days	20 [6]
Tufts Medical School Postgraduate Division, 30 Bennet Street, Boston At: Boston City Hospital	Dermatology B	April 14-18, 1947	30 [1]
University of Minnesota Medical School, Department of Postgraduate Education, Minneapolis 14	Continuation Course in Pathology of Skin Diseases	Jan. 21-Feb. 20, 1947, 1 month	50
University of Buffalo School of Medicine, 24 High Street, Buffalo	Dermatology and Syphilology (Seminar)	April, 1947, 3 days	Not given

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
DERMATOLOGY AND SYPHILOLOGY—Continued			
Columbia University, 630 West 168th Street, New York 32 At: Mount Sinai Hospital	Venereal and Skin Diseases	March 24-27, 1947, 4 days, part time	20
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Symposium on Dermatology and Syphilology [5]	May 12-17, 1947, 5 days, full time	90
	Seminar in Dermatological Histopathology [5]	May 19-23, 1947, 5 days, full time	60
New York Polyclinic Medical School and Hospital, 341 West 50th Street, New York 19	Dermatology and Syphilology	First of any month, 6 weeks, part time	100
New York Polyclinic Medical School and Hospital	Dermatology and Syphilology	First of any month, 3 months, part time	150
New York University College of Medicine, 477 First Avenue, New York 16	Industrial Dermatology	Spring, 1947, 3 weeks, part time for 2 weeks, full time for 1 week	100
At: Beth Israel Hospital	Dermatology	Jan. 6, 1947, 4 weeks, part time, 2 days a week	25
	Dermatology	March, 1947, 4 weeks, part time, 2 days a week	25
	Dermatology	April, 1947, 4 weeks, part time, 2 days a week	25
DIABETES			
University of Southern California, Division of Graduate Medicine, 3551 University Avenue, Los Angeles 7 At: Los Angeles County Hospital	Diabetes Mellitus, Course No. 739 (Lectures)	March 31, 1947, 6 weeks, 1 evening a week	$ 50 [1]
Harvard University Medical School, 25 Shattuck St., Boston At: Deaconess Hospital	Diabetes Mellitus and Its Relation to General Medicine	April 7-9, 1947, 3 days	Not given
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Diabetes Mellitus, Nephritis and Hypertension	Jan. 9-Feb. 27, 1947, 2 months, part time	45
	Diabetes Mellitus, Nephritis and Hypertension	March 24-28, 1947, 5 days, full time	45
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2 At: Greenpoint Hospital At: Jewish Hospital	Diabetes Mellitus and Its Complications	April 10, 1947, 12 sessions, once a week, part time	20
	Diabetes	April 17, 1947, 8 sessions, once a week, part time	20
University of Pennsylvania Graduate School of Medicine, 237 Medical Laboratories, Philadelphia 4 At: Philadelphia Hospital	Diabetes Mellitus	Arranged, 2 weeks, 75 hours	150
ELECTROCARDIOGRAPHY			
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Personal Course in Heart Disease and Electrocardiography	To be announced, 10 weeks, part time, 1 day each week	$125
	Electrocardiography and Heart Disease	To be announced, 1 month, full time	175
Michael Reese Hospital Postgraduate School, 29th Street and Ellis Avenue, Chicago 16 At: Michael Reese Hospital	Electrocardiographic Interpretation for Graduate Physicians	Feb. 12, 1947, 12 weeks, part time, each Wednesday	50
Tufts Medical School Postgraduate Division, 30 Bennet Street, Boston At: Pratt Diagnostic Hospital	I Electrocardiography	March 24-28, 1947, 1 week, full time	40
	II Electrocardiography II	Jan. 13-15, 1947	25
Columbia University, 630 West 168th Street, New York 32 At: Mount Sinai Hospital	Intensive Course in Clinical Electrocardiography	April 14-19, 1947, 5 days, full time	40
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Electrocardiography	March 17-21, 1947, 5 days, full time	50
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2 At: Beth El Hospital	Electrocardiography and Heart Sound Recording	April 8, 1947, 8 sessions, twice a week, part time	20
At: Jewish Hospital	Clinical Electrocardiography	April 14, 1947, 15 sessions, 3 times a week, part time	20
	Electrocardiography and Clinical Cardiography	April 15, 1947, 15 sessions, 3 times a week, part time	20
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Electrocardiography	Spring, 1947, 2 weeks, part time	100
New York Polyclinic Medical School and Hospital, 341 West 50th Street, New York 19	Electrocardiographic Interpretation	Arranged, 2 weeks, 2 hours daily	75
New York University College of Medicine, 477 First Avenue, New York 16 At: Bellevue Hospital and College of Medicine At: Beth Israel Hospital	Advanced Electrocardiography	March 3, 1947, 16 weeks, 2 hours a week	100
	Electrocardiography	Feb. 20, 1947, 12 weeks, part time	40
University of Oregon Medical School, West Marquam Hill Road, Portland 1, Ore.	Electrocardiography	June 2-6, 1947 5 days, full time	50
University of Pennsylvania Graduate School of Medicine, 237 Medical Laboratories, Philadelphia 4 At: Philadelphia Hospital	Electrocardiology and Cardiac Roentgenology [7]	Not given, 5 days, 30 hours	60
University of Texas Medical Branch, 912 Avenue B, Galveston, Texas.	Electrocardiography	Feb. 3-8, 1947, 1 week, afternoons	Not given
ELECTROENCEPHALOGRAPHY			
University of Illinois College of Medicine, 1853 West Polk Street, Chicago	Electroencephalography	Arranged, 3 weeks, full time	$ 50
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Clinical Electroencephalography [5]	March 3-28, 1947, 4 weeks, part time, Monday and Friday	60
University of Pennsylvania Graduate School of Medicine, 237 Medical Laboratories, Philadelphia 4 At: Graduate Hospital of Pennsylvania Institute	Electroencephalography	Arranged, 6 Thursdays, 36 hours	150
ENDOCRINOLOGY			
College of Medical Evangelists, 312 North Boyle Avenue, Los Angeles 33 At: White Memorial Hospital	Practical Endocrinology	Feb. 13, 1947, 6 weeks, 6 hours, Thursday evening	20
Tufts Medical School Postgraduate Division, 30 Bennet Street, Boston At: Pratt Diagnostic Hospital	Endocrinology	May 26-30, 1947, 1 week, full time	$ 40
University of Michigan Medical School, Department of Postgraduate Medicine, 1313 East Ann Street, Ann Arbor, Mich.	Endocrinology and Metabolism	Spring, 1947	15
Columbia University, 630 West 168th Street, New York 32 At: Mount Sinai Hospital	Endocrinological Diseases	March 24-29, 1947, 5 days, part time	20
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2 At: Jewish Hospital	Disorders of the Endocrine System	April 14, 1947, 8 sessions, twice a week	20
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Endocrinology	May, 1947, 2 weeks, full time	150
	Physiology of the Endocrine System	Mid-winter and spring, one month, arranged	75
Duke University School of Medicine, Durham, N. C.	Endocrinology	Arranged, 3 months or longer, full time	150 per qtr.

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	ENDOSCOPY		
Colorado State Medical Society, Republic Building, Denver At: Shirley Savoy Hotel	Bronchoscopy	Feb. 19-21, 1947 (Indefinite)	None [1]
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Practical Cystoscopy	Jan. 28, 1947 and every 2 weeks thereafter, 2 weeks, full time	$150
University of Illinois College of Medicine, 1853 West Polk Street, Chicago	Bronchoesophagology and Laryngeal Surgery	Feb., 1947, 2 weeks, full time	150
	Bronchoesophagology and Laryngeal Surgery	May, 1947, 2 weeks, full time	150
Columbia University, 630 West 168th Street, New York 32 At: Columbia Presbyterian Medical Center	Bronchoscopy [5]	April 21-May 9, 1947, 3 weeks, part time	250
	Gastroscopy [5]	Arranged, 2 months, 3 times a week	250
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Cystoscopy and Endoscopy	Jan. 3, 1947, 15 sessions, part time	75
	Cystoscopy and Endoscopy	Jan. 6, 1947, 15 sessions, part time	75
	Cystoscopy and Endoscopy	Feb. 17, 1947, 15 sessions, part time	75
	Cystoscopy and Endoscopy	Mar. 3, 1947, 15 sessions, part time	75
	Cystoscopy and Endoscopy	April 7, 1947, 15 sessions, part time	75
	Cystoscopy and Endoscopy	May 2, 1947, 15 sessions, part time	75
	Cystoscopy and Endoscopy	May 19, 1947, 15 sessions, part time	75
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Gastroscopy	Arranged, 2 weeks, full time	200
New York University College of Medicine, 477 First Avenue, New York 16 At: New York Eye and Ear Infirmary	Peritoneoscopy	Arranged	100
	Broncho-Esophagology [5]	April, 1947, 16 days; part time for 12 days, full time for 4 days	250 [8]
Temple University School of Medicine, 3400 North Broad Street, Philadelphia	Laryngology and Broncho-Esophagology	Arranged, probably Feb., 1947; 2 weeks (60 hours)	250
	Laryngology and Broncho-Esophagology	Arranged, probably April, 1947; 2 weeks (60 hours)	250
University of Pennsylvania Graduate School of Medicine, 237 Medical Laboratories, Philadelphia 4 At: Graduate Hospital	Bronchoesophagology, Gastroscopy and Laryngeal Surgery	Arranged, 2 weeks, 85 hours	250
	Cystoscopy, Chromoureteroscopy and Pyelography	Arranged, 6 weeks, 36 hours	300
	FRACTURES		
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Intensive Course in Fractures	April 28, 1947, 2 weeks, full time	$125
	Intensive Course in Fractures	June 23, 1947, 2 weeks, full time	125
	Special Course in Fractures	To be announced, 10 weeks, part time	125
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2 At: Kings County Hospital	Fractures	April 5, 1947, 10 sessions, once weekly, part time	20
New York Medical College Flower and Fifth Avenue Hospitals, 1 East 105th St., New York	Fractures and Allied Trauma	Fall and Spring, 1947, 3 weeks, full time	150
	GASTROENTEROLOGY		
University of Southern California, Division of Graduate Medicine, 3551 University Avenue, Los Angeles 7 At: Los Angeles County Hospital	Gastroenterology, Course No. 741	May 12, 1947, 12 evening lectures, 1 evening weekly	$ 50 [1]
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Personal Course in Gastroscopy and Gastroenterology	March 24, 1947, 2 weeks, full time	200
	Personal Course in Gastroscopy and Gastroenterology	May 19, 1947, 2 weeks, full time	200
Tulane University of Louisiana School of Medicine, 1430 Tulane Avenue, New Orleans 13	Gastrointestinal Diseases	Jan. 20-25, 1947, 5½ days, full time	25
Maine Medical Association, 177c Main Street, Waterville, Me. At: Boston	Gastroenterology	Arranged, 1-2 weeks	Arranged [2]
University of Michigan Medical School, Department of Postgraduate Medicine, 1313 East Ann Street, Ann Arbor, Mich.	Gastroenterology	Spring, 1947, 1 week	30
University of Buffalo School of Medicine, 24 High Street, Buffalo	Gastroenterology (Seminar)	March, 1947, 3 days	Not given
Columbia University, 630 West 168th Street, New York 32 At: Mount Sinai Hospital	Gastro-intestinal Diseases	Feb. 3-March 11, 1947, 5 weeks, part time	75
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Gastroenterology	Jan. 8-Feb. 26, 1947, 2 months, part time, Wednesdays	45
	Gastroenterology	April 7-18, 1947, 10 days, full time	75
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2 At: Greenpoint Hospital At: Jewish Hospital	Gastroenterology	April 16, 1947, 12 sessions, twice weekly	20
	Gastroenterology	April 8, 1947, 8 sessions, twice weekly, part time	20
New York Medical College Flower and Fifth Avenue Hospitals, 1 East 105th St., New York	Gastroenterology	Arranged, 1 month	100
	Physiology and Chemistry of the Gastrointestinal Tract, Digestion	Arranged, 1 month	150
New York Polyclinic Medical School and Hospital, 341 West 50th Street, New York 19	Gastroenterology	Jan., 1947, 6 weeks, part time	50
	Gastroenterology	April, 1947, 6 weeks, part time	50
New York University College of Medicine, 477 First Avenue, New York 16 At: Bellevue Hospital At: Beth Israel Hospital	Clinical Gastroenterology	Feb. 19, 1947, 20 weeks, part time, 1 day a week	100
	Gastroenterology	Jan. 6, 1947, 8 weeks, part time, Monday and Friday	55
At: Lenox Hill Hospital	Gastroenterology	Winter, 1947, 7 weeks, part time, 2 mornings a week	50
	Gastroenterology	Spring, 1947, 7 weeks, part time, 2 mornings a week	50
University of Pennsylvania Graduate School of Medicine, 237 Medical Laboratories, Philadelphia 4 At: Graduate Hospital	Clinical Gastroenterology [7]	Arranged, 16 weeks, 500 hours	400
University of Wisconsin Medical School, 418 North Randall Madison 6, Wis.	Observation Course in Gastroenterology	Feb., 1947, 5 days, full time	25
	HEMATOLOGY		
University of Southern California, Division of Graduate Medicine, 3551 University Avenue, Los Angeles 7 At: Los Angeles County Hospital	Hematology, Course No. 738	Jan. 6, 1947, 12 weeks, 1 evening a week	$ 50 [1]
Tufts Medical School Postgraduate Division, 30 Bennet Street, Boston	Hematology C	June 9-22, 1947, 2 weeks, full time	100
Columbia University, 630 West 168th Street, New York 32 At: Montefiore Hospital	Clinical Hematology	Feb. 4-June 17, 1947, 20 weeks, part time	75
At: Mount Sinai Hospital	Hematology	Feb. 17-March 15, 1947, 4 weeks, part time	50

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
HEMATOLOGY—Continued			
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Clinical Hematology	Jan. 8-Feb. 26, 1947, 2 months, part time	30
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Street, Brooklyn 2 At: Jewish Hospital	Clinical Hematology	April 17, 1947, 8 sessions, once weekly, part time	Not given
New York Medical College Flower and Fifth Avenue Hospitals, 1 East 105th St., New York	Hematology	Spring, 1947, 2 months, Tuesday afternoons	50
New York University College of Medicine, 477 First Avenue, New York 16 At: Lenox Hill Hospital	Hematology	Spring, 1947, 6 weeks, part time	50
HOSPITAL ADMINISTRATION			
University of Minnesota Medical School, Department of Postgraduate Education, Minneapolis 14 At: Center for Continuation Study	Continuation Course in Hospital Administration [9]	Feb. 3-8, 1947, 1 week	Not given
INDUSTRIAL HEALTH			
Yale University School of Medicine, 333 Cedar Street, New Haven, Conn.	Advanced Industrial Medicine	Feb. 4, 1947 (beginning), 10 sessions	$ 10
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Symposium on Industrial Medicine	June 9-13, 1947, 5 days, full time	45
University of Pittsburgh School of Medicine, Pittsburgh	Industrial Hygiene Engineering	Second semester of college year, 16 weeks, part time	20
	Industrial Toxicology	Second semester of college year, 16 weeks, part time	Not given
Wisconsin State Board of Health, Industrial Hygiene Institute, State Office Bldg., 1 W. Wilson St., Madison 2, Wis. At: Three cities in Wisconsin (to be selected)	Industrial Health Clinic	Probably May 1947	None
MALIGNANT DISEASES			
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33 At: White Memorial Hospital	Malignant Tumors	Jan. 15, 1947, 10 weeks, one evening week	30
University of Kansas School of Medicine, 39th Street and Rainbow Boulevard, Kansas City, Kan.	Radiology and Cancer	June 9-13, 1947, 5 days	$ 20 [6]
University of Minnesota Medical School, Department of Postgraduate Education, Minneapolis 14	Continuation Course in Cancer for Physicians	Jan. 2-4, 1947, 3 days	15
MEDICINE, GENERAL			
University of Alabama School of Medicine, University, Ala.	Medicine	March, 1947, 1 week	None
Los Angeles County Tuberculosis and Health Association, 117 West Ninth Street, Los Angeles 15	Postgraduate Medical Symposium for Negro Physicians (Essentially)	March 10-14, 1947, 4 days (8 hours)	None
Research Study Club of Los Angeles, Inc., 727 West 7th Street, Los Angeles At: Elk's Club	Sixteenth Annual Mid-Winter Postgraduate Clinical Convention	Jan. 29-Feb. 4, 1947, 2 weeks—clinical; 5 days—cadaver	$ 75 en. course
University of Southern California, Division of Graduate Medicine, 3551 University Avenue, Los Angeles 7	Clinical Review of Internal Medicine	Jan. 6, 1947, 12 weeks, full time	250 [1]
	Clinical Review of Internal Medicine (Course 730)	May 5, 1947, 12 weeks, full time	250 [1]
At: Los Angeles County Hospital	Nine-Month Internal Medicine Course (731)	Following course 730, 9 months	750 [10]
	Recent Advances in Diagnosis and Treatment, Course No. 743	Jan. 2, 1947, 3 periods, 12 weeks, each Thursday evening	Not given
	Recent Advances in Diagnosis and Treatment, Course No. 743	March 27, 1947, 3 periods, 12 weeks, each Thursday evening	Not given
University of California Medical School, University Extension, San Francisco 22	Course in Internal Medicine and General Surgery (for General Pract.)	Feb. 10-14, 1947, 5 days, full time	Not given
College of Medical Evangelists, 312 North Boyle Avenue, Los Angeles 33 At: White Memorial Hospital	Varicose Veins	Feb. 4 and 11, 1947, 2 evenings	15
	General Medicine	Feb. 6, 1947, 10 weeks, 1 eve. a wk.	35
Colorado State Medical Society, Republic Building, Denver At: Shirley Savoy Hotel	Internal Medicine	Feb. 19-21, 1947 (indefinite)	None [1]
George Washington University School of Medicine, 1335 H St., N.W., Washington 5, D. C.	Intensive Postgraduate Course in Diseases of Metabolism	Feb. 10-14, 1947, 1 week, full time	$ 50
	Intensive Postgraduate Course in General Medicine	Feb. 10-March 7, 1947, 4 weeks, full time	200
	Intensive Postgraduate Course in Thoracic Diseases	March 3-7, 1947, 1 week, full time	50
At: Affiliated Hospitals	Intensive Refresher Course in Infectious Diseases	Feb 24-28, 1947, 1 week, full time	50
	Intensive Postgraduate Course in Internal Medicine	Feb. 10-March 14, 1947, 5 weeks, full time	250
Medical Society of the District of Columbia, 1718 M St., N.W., Washington, D. C.	Postgraduate Course in Diagnosis	Feb. 4, 11, 18, 1947 (3 lectures)	1
Emory University Medical School, 50 Armstrong St., Atlanta, Ga. At: Affiliated Hospitals	General Internal Medicine	Arranged individually, 2 weeks to 3 months or longer, full time	125 per qtr. 12 per wk.
University of Georgia School of Medicine, University Place, Augusta, Ga.	Postgraduate Course for Negro Physicians	June 17-21, 1947, 5 days	None
	General Refresher	Intermittently, 3 weeks-3months	50 res. 75 non-res.
American College of Physicians, 4200 Pine St., Philadelphia 4 At: Chicago Institutions	28th Annual Session, American College of Physicians	April 28-May 2, 1947, 1 week	12 non-mem None mem.
Chicago Medical Society, 30 N. Michigan Ave., Chicago	Third Clinical Conference	March 4-7, 1947, 4 days	Not given
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	2 weeks Course in Internal Medicine	April 7, 1947, 2 weeks, full time	75
	2 weeks Course in Internal Medicine	June 2, 1947, 2 weeks, full time	75
University of Illinois College of Medicine, 1853 West Polk Street, Chicago	Refresher Course in General Practice for Veteran Physicians	Arranged, 3 mo., full time	75 res. 100 non-res.
St. Elizabeth Hospital, LaFayette, Ind.	Postgraduate Medical Four Year Extension Course	First Tuesday of every mo., 3 hours per mo., 12 mo. per year	None
State University of Iowa School of Medicine, Iowa City	Informal Refresher Courses	Jan.-June, 1947, 6 mo., part time	None
	Physician's Monthly Clinical Conference	March 24-29, 1947, 6 days	None
	Physician's Monthly Clinical Conference	April 28-May 3, 1947, 6 days	None
	Physician's Monthly Clinical Conference	May 26-31, 1947, 6 days	None
	Physician's Monthly Clinical Conference	June 23-28, 1947, 6 days	None

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
MEDICINE, GENERAL—Continued			
University of Kansas School of Medicine, 39th and Rainbow Blvd., Kansas City 3, Kan. At: University of Kansas Hospitals	Internal Medicine and Dermatology	March 17-21, 1947, 5 days	20 [9]
Kentucky State Medical Association, 620 S. Third Street, Louisville, Ky.	Refresher Course in Internal Medicine	January 1947, 6 weeks continuously	None
	Refresher Course	Continuously, 6 weeks	None
Flint-Goodridge Hospital of Dillard University, New Orleans	Postgraduate Course for Physicians	June 23-28, 1947, 6 days, full time	Not given
New Orleans Graduate Medical Assembly, 1430 Tulane Ave., New Orleans 13 At: Municipal Auditorium	Tenth Annual Meeting	Feb. 24-27, 1947, 4 days	Not given
Tulane University of Louisiana School of Medicine, 1430 Tulane Avenue, New Orleans 13	General Refresher Course	Jan. 6-April 12, 1947, 1 week or more, full time	25 per wk.
	Review of General Medical Practice	Jan. 6-Feb. 8, 1947, 1 mo.	Not given
	Review of General Medical Practice (Continued)	March 3-April 12, 1947, 6 weeks	Not given
	Infectious Diseases	March 31-April 5, 1947, 5½ days, full time	25
	Nutritional and Metabolic Diseases	March 24-29, 1947, 5½ days	25
Mississippi State Board of Health, Jackson, Miss. At: Tulane University of Louisiana, New Orleans	Neoplastic diseases	April 7-12, 1947, 6 days	None [11]
American College of Physicians, 4200 Pine St., Philadelphia 4 At: Tufts Medical School, Boston	Blood Disorders	Spring 1947, 1 week	20 mem. 40 non-mem.
The Lahey Clinic, 605 Commonwealth Ave., Boston At: New England Mutual Hall, Boston	Postgraduate Assembly	Jan. 13-16, 1947, 3 days, full time	25 [12]
Massachusetts Medical Society, 8 The Fenway, Boston At: Boston and various parts of state	Postgraduate Instruction	Throughout year	None
	Review Lecture Course for Practitioners and Former Medical Officers	Feb. 18-May 15, 1947, 3 mo., part time, 2 evenings a week	Not given
Tufts Medical School Postgraduate Division, 50 Bennet Street, Boston At: Boston Dispensary and Pratt Diagnostic Hospital,	Clinical Medicine	Feb. 3-March 1, 1947, 4 weeks	50
	Diseases of the Bone and Joints	March 17-21, 1947, 5 days, full time	40 [1]
	General Refresher	April 7-June 28, 1947, 12 weeks, full time	300
	Internal Medicine	Arranged, 1 year or 6 mo.	800 per yr.
	Internal Medicine	April 7-May 2, 1947, 1 mo., full time	100
	Mixed Service	April 1947, 1 year, full time	500 [1]
	Application of the Basic Sciences to Clinical Medicine	March 3-April 26, 1947, 8 weeks, full time	200
	Clinical Internal Medicine	Feb. 6-April 24, 1947, part time, Thursdays	50
University of Michigan Medical School, Department of Postgraduate Medicine, 1313 East Ann Street, Ann Arbor, Mich.	Course for Practitioners	Feb. 3-28, 1947, 4 weeks, full time	100
	Diseases of the Blood and Blood-Forming Organs	Spring 1947, 1 week	30
	Internal Medicine	March-April, 1947, 2 mo.	50 per mo.
	Practitioners' Course	Spring, 1947, 2 days	None
At: University of Michigan Hospital	Personal Courses	Throughout year, varying lengths	30 per mo.
American College of Physicians, 4200 Pine St., Philadelphia 4 At: University of Michigan Medical School, Ann Arbor, Mich.	Internal Medicine	April 7-19, 1947, 2 weeks	40 mem. 80 non-mem.
University of Michigan Medical School, Department of Postgraduate Medicine, 1313 East Ann Street, Ann Arbor, Mich. At: Battle Creek-Kalamazoo, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Bay City, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Flint, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Grand Rapids, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Houghton, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Ironwood, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Jackson-Lansing, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Marquette, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Powers, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Saginaw, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Traverse City, Mich.	Practitioners' Course	Spring 1947, 2 days	None
At: Upper Peninsula, Mich.	Practitioners' Course	Spring 1947, 2 days	None
	Conferences in Medical Technology	Jan. 31-Feb. 1, 1947, 2 days	Not given
	Conferences in Medical Technology	March 14-15, 1947, 2 days	Not given
	Conferences in Medical Technology	April 11-12, 1947, 2 days	Not given
University of Minnesota Medical School, Department of Postgraduate Education, Minneapolis At: Center for Continuation Study	Conferences in Medical Technology	May 2-3, 1947, 2 days	Not given
	Conferences in Medical Technology	May 23-24, 1947, 2 days	Not given
	Conferences in Medical Technology	June 6-7, 1947, 2 days	Not given
	Medicine	To be announced, 3 days	15
	Medicine	To be announced, 6 days	25
	Medicine	To be announced, 12 days	50
Mississippi State Sanatorium, Sanatorium, Miss.	Internal Medicine	Continuously, all year, 2 weeks	None
Creighton University School of Medicine, 306 North 14th Street, Omaha	Internal Medicine	Continuously, all year, 6 mo.	None
	General Medicine	Arranged, 3 mo.	None
	Special Courses	Individually arranged, 3 mo.	None
University of Nebraska College of Medicine, 42nd St. and Dewey Ave., Omaha At: Beatrice, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: Chadron, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: Grand Island, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: Hastings, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: Kearney, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: McCook, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: Norfolk, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: North Platte, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None

References will be found on page 946.

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
MEDICINE, GENERAL—Continued			
At: Scottsbluff, Neb.	Extramural Continuation Courses	Arranged, 1 day afternoon clinics, evening lectures	None
At: Omaha, Neb.	Intramural Continuation Courses	Arranged, 1 and 2 weeks	None
Rutgers University, New Brunswick, N. J. At: Cooper Hospital, Camden, N. J.	Rutgers Plan, Postgraduate Medical Course	Jan. 1, 1947, and every qtr., part time, 66 hours per qtr.	24 per qtr.
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2	Sterility	April 8, 1947, 12 sessions, once weekly, part time	20
At: Greenpoint Hospital	Hypertension and Nephritis	April 9, 1947, 8 sessions, once weekly, part time	20
At: Jewish Hospital	Peripheral Vascular Diseases	April 14, 1947, 8 sessions, once weekly, part time	20
Cornell University Medical College, 1300 York Ave., New York At: Bellevue Hospital	Six Months' Postgraduate Course in Internal Medicine	First of each month, 6 mo.	250
	2 Weeks' Refresher Course Internal Medicine	April 1-14, 1947, 2 weeks	50
Columbia University, 630 West 168th Street, New York 32 At: Montefiore Hospital	Peripheral Vascular Diseases	April 1-June 29, 1947, 3 mo. Feb. 24-June 27, 1947, 18 weeks, part time	55 per mo. 75
At: Mount Sinai Hospital	Diseases of the Kidneys	Feb. 17-21, 1947, 5 days, part time	10
	Diseases of the Liver	Feb. 3-20, 1947, 18 days, part time	20
	Diseases of Metabolism	March 12-25, 1947, 13 days, part time	20
	Geriatrics	March 27, 1947, 8 weeks, part time	50
	Symposium on Internal Medicine	Feb. 3-March 29, 1947, 8 weeks, full time	200
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Diseases of the Liver and Biliary Tract	Jan. 8-Feb. 26, 1947, 2 mo., part time	30
	Diseases of the Liver, Biliary Tract and Pancreas—Introductory Course	May 7-June 11, 1947, 5 weeks, part time	60
	Diseases of the Thyroid and Other Endocrine Glands, and Disorders of Nutrition	Jan. 10-Feb. 28, 1947, 2 mo., part time, Fridays	45
	Peripheral Vascular Diseases	Jan. 7-Feb. 25, 1947, 2 mo., part time, Tuesdays	30
	Peripheral Vascular Diseases	April 28-May 2, 1947, 5 days, full time	45
	Problems in Diagnosis	Jan. 6-Feb. 24, 1947, 2 mo., part time, Mondays	45
	Psychological Aspects of Internal Medicine	Jan. 10-Feb. 28, 1947, 2 mo., part time, Fridays	25
	Seminar in Internal Medicine	Jan. 6-Feb. 28, 1947, 2 mo., full time	225
	Symposium on Internal Medicine	June 16-27, 1947, 10 days, full time	75 [13]
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th Street, New York	Immunology	Arranged	50
	Internal Medicine	Monthly, 1 mo.	150
	Parasitology	Arranged	75
	Peripheral Vascular Diseases	Spring 1947, 2 mo., 2 half days a week	100
New York Polyclinic Medical School and Hospital, 341 West 50th Street, New York 19	Course for General Practitioners	Jan. 1, 1947, 6 weeks	100
	Course for General Practitioners	Jan. 1947, 3 mo.	200
	Course for General Practitioners	Feb. 15, 1947, 6 weeks	100
	Course for General Practitioners	Feb. 15, 1947, 3 mo.	200
	Course for General Practitioners	April 1, 1947, 6 weeks	100
	Course for General Practitioners	April 1, 1947, 3 mo.	200
	Course for General Practitioners	May 15, 1947, 6 weeks	100
	Course for General Practitioners	May 15, 1947, 3 mo.	200
	Courses in Forensic Medicine	January through June, 1947, Variable	Variable
New York University College of Medicine, 477 First Avenue, New York 16 At: Bellevue Hospital	General Review for General Practitioners	Jan. 6-April 3, 1947, 12 weeks, full time	175 vets. 225 non-vets.
	Internal Medicine	Jan. 6, 1947, 12 weeks, part time	150
	Internal Medicine	April 3, 1947, 12 weeks, part time	150
At: Lenox Hill Hospital	General Review for General Practitioners	Spring 1947, 8 weeks, full time	125
New York University College of Medicine, 477 First Avenue, New York 16	Mycology	Jan. 1947, 8 weeks, Monday, Wednesday, Thursday, part time	50
University of North Carolina School of Medicine, Extension Department, Chapel Hill, N. C. At: Various towns in North Carolina	University Postgraduate Course in Clinical Medicine	Winter 1947, 1 day a week for 8 weeks	Not given
	University Postgraduate Course in Clinical Medicine	Spring 1947, 1 day a week for 8 weeks	Not given
Duke University School of Medicine, Durham, N. C.	General Medicine	Arranged, full time, 1 or 2 weeks or longer	150
	Medicine	Arranged, 3 mo. or longer, full time	150 per qtr.
American College of Physicians, 4200 Pine St., Philadelphia 4 At: University of Cincinnati School of Medicine, Cincinnati	Internal Medicine with Emphasis Upon Nutrition and Metabolism	May 26-June 7, 1947, 2 weeks	40 mem. 80 non-mem.
Cleveland Clinic, Euclid Ave. at 93rd St., Cleveland	Blood and the Blood Vessels	Not given, 3 days, full time	10
Ohio State Medical Association, 1005 Hartman Theater Building, Columbus 15, O.	Ohio State Medical Association, Annual Meeting (Lectures)	May 6-8, 1947, 3 days	None
Ohio State University College of Medicine, 11th and Neil Avenues, Columbus, O. At: University Hospital	Refresher Course in General Medicine for General Practitioners	March 17-22, 1947, 5½ days	20
University of Oregon Medical School, West Marquam Hill Road, Portland 1, Ore.	Special Refresher Course	Arranged, individually, full or part time	75 per mo.
American College of Physicians, 4200 Pine St., Philadelphia 4 At: Lankenau Hospital	Problems in Growth and Aging	Feb. 3-7, 1947, 1 week	20 mem. 40 non-mem.
Philadelphia County Medical Society, 201 S. 21st St., Philadelphia At: Bellevue-Stratford Hotel	Progress in Medicine	April 15-18, 1947, 4 days, full time	Mem. none 5 non-mem.
University of Pittsburgh School of Medicine, Bigelow Boulevard, Pittsburgh At: Medical Center	Refresher Course for General Practitioners	Jan. 28-March, 1947, 8 weeks	150
	Refresher Course for General Practitioners	April 22-May 25, 1947, 5 weeks	100
Tennessee State Medical Association, Doctors Building, Nashville 3, Tenn.	Five Courses on Postgradute Instruction	Continuously, 10 meetings, 2 hours each	Not given
Vanderbilt University School of Medicine, Division of Postgraduate Instruction, 21 Avenue So. at Edgehill, Nashville, Tenn.	Medicine	May-Oct. 1947, 1 to 3 mo., full time	166.66 3 mos.

References will be found on page 946.

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
MEDICINE, GENERAL—Continued			
University of Texas Medical Branch, Galveston, Tex.	Internal Medicine	Feb. 3-8, 1947, 1 week	Not given
	Fundamental Medical Science (Review of recent advances in the Preclinical Sciences)	Feb. 24-March 1, 1947, 1 week	Not given
	Tumor Conference	March 8, 1947, 1 day	5
	Tumor Conference	June 14, 1947, 1 day	5
University of Vermont College of Medicine, Pearl St., College Park, Burlington, Vt.	Course for General Practice	Arranged, throughout year, 12 weeks, 3-5 hours daily	750 per yr. [14]
	Course in Internal Medicine	Throughout year, min. 4 weeks, 3-5 hours daily	750 per yr.[14]
	General Practice; Internal Medicine, Surgery	Throughout year, beginning of any month, 1-9 mo.	750 per yr.[14]
Medical College of Virginia, 12th and Marshall Sts., Richmond, Va.	St. Philip Hospital Postgraduate Clinic for Negro Physicians	June 1947, 2 weeks	None res. 5 non-res.
The Medical Society of Milwaukee County, 202 East Wisconsin Avenue, Milwaukee At: Marquette University School of Medicine At: Various Hospitals	Postgraduate Course in Internal Medicine	February 1947, 4 weeks	Not given
	Postgraduate Course in Internal Medicine	Third week in May 1947, 4 weeks	Not given
University of Wisconsin Medical School, 418 North Randall Street, Madison 6, Wis.	Observation Course for Specialists (Medicine and Surgery)[5]	Continuous, 1947, 2-6 mo.	100 per mo.
	Postgraduate Course in Thoracic Diseases [5]	March 3-8, 1947, 1 week	50
NEUROLOGY AND PSYCHIATRY			
College of Medical Evangelists, 312 North Boyle Avenue, Los Angeles 33 At: White Memorial Hospital	Medical Psychology	April 3, 1947, 10 periods, 1 evening a week	20
University of Southern California, Division of Graduate Medicine, 3551 University Ave., Los Angeles 7 At: Los Angeles County Hospital	Psychosomatic Medicine, Course No. 742	Jan. 8, 1947, 12 2-hour lectures, 1 evening weekly	50 [1]
Colorado State Medical Society, Republic Building, Denver At: Shirley Savoy Hotel	Internal Medicine	Feb. 19-21, 1947 (indefinite)	None [1]
Catholic University of America, Department of Psychology and Psychiatry, Washington, D. C. At: St. Elizabeth's Hospital	Individual Clinical Conferences	January 1947, 1 sem., 2 hours a week	200 per sem. 20 per wk.
	Psychopathology	January 1947, 1 sem., 2 hours a week	200 per sem. 20 per wk.
	Case Seminar in Psychotherapy	January 1947, 1 sem., 2 hours a week	200 per sem. 20 per wk.
	Introduction to Psychiatry	January 1947, 1 sem., 2 hours a week	200 per sem. 20 per wk.
	Clinical Psychiatry	January 1947, 1 sem., 2 hours a week	200 per sem. 20 per wk.
	Electric Shock Therapy	January 1947, 1 sem., 2 hours a week	200 per sem. 20 per wk.
	Individual Psychotherapy	Not given	Not given
	Neurology and Neuropathology	January 1947, 1 sem., 2 hours a week	200 per sem. 20 per wk.
	Intensive Postgraduate Course in Psychiatry	Feb. 24-March 7, 1947, 2 weeks, full time	100
George Washington University School of Medicine, 1335 H St., Washington 5, D. C. At: St. Elizabeth's Hospital	Intensive Postgraduate Course in Neurology and Neurosurgery	March 10-14, 1947, 1 week, full time	50
	Intensive Postgraduate Course in Psychiatry and Neurology	Feb. 24-March 14, 1947, 3 weeks, full time	150
	Intensive Postgraduate Course in Psychiatry	Feb. 24-March 7, 1947, 2 weeks, full time	100
	Psychiatric Conferences	January-July 1, 1947, 2 sem., 1 hour a week	200 per sem. 10 per wk.
Tulane University of Louisiana School of Medicine, 1430 Tulane Avenue, New Orleans 13	Nervous System Diseases	March 17-22, 1947, 5½ days,, full time	25
Metropolitan State Hospital, Waltham, Mass. At: Boston Psychopathic Hospital, Boston	Twelfth Postgraduate Seminar in Neurology and Psychiatry	March 19-May 14, 1947, 2 mo., 1 day per week, 5:30 to 10 p. m.	None
Metropolitan State Hospital, Waltham, Mass. At: Walter E. Fernald State School, Waverly, Mass.	Twelfth Postgraduate Seminar in Neurology and Psychiatry	Jan. 3-April 25, 1947, 1 day a week, 2-10 p. m.	None
	Pediatric Neuropsychiatry (Child Psychiatry)	March 17-May 12, 1947, 2 mo., 1 day per week, 5:30 to 10 p. m.	None
American Institute for Psychoanalysis, 266 West End Ave., New York 23	The Analytic Process [5]	Feb. 7, 1947, 15 weekly sessions	30
	Problems in the Patient-Analyst Relationship [5]	Every other week, beginning Feb. 27, 1947, every week from May 1, 14 weeks	20
At: New School for Social Research	At War with Ourselves: Self-acceptance and Self-condemnation	Feb. 3, 1947, 15 weekly lectures	25
	Confronting the Modern World: Problems of Children and Adolescents	Feb. 4, 1947, 15 weekly lectures	15
Columbia University, 630 West 168th Street, New York 32 At: Montefiore Hospital At: Mount Sinai Hospital	Review of Neuropsychiatry	April 14-May 9, 1947, 4 weeks, full time	100
	Recent Advances in Neurology and Psychiatry	March 31-April 4, 1947, 5 days, full time	40
Columbia University—At: New York Postgraduate Medical School, 303 East 20th Street, New York 3	Neurological and Psychiatric Diagnosis and Treatment in General Practice	March 17-29, 1947, 2 weeks, full time	75
	Psychoanalysis in General Medicine	Jan. 6-March 26, 1947, 12 sessions, part time, Wednesdays	50
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th St., New York	Neurology	Spring 1947, 1 mo., full time	200
	Psychoanalysis and Psychiatry	Feb. 7-May 16, 1947, Friday eves., 15 hours	40
New York University College of Medicine, 477 First Avenue, New York 16 At: Lenox Hill Hospital	Neurology	Spring 1947, 6 weeks, part time 3 afternoons a week	75
	Psychiatry	Spring 1947, 6 weeks, part time, 2 afternoons a week	60
Duke University School of Medicine, Durham, N. C.	Neuropsychiatry	Arranged, 3 mo. or longer, full time	150 per qtr.
University of Pennsylvania Graduate School of Medicine, 237 Medical Laboratories, Philadelphia 4 At: Philadelphia Hospital At: Medical Laboratories and Affiliated Institutions	Clinical Psychiatry	Arranged, 8 weeks, 240 hours	160
	Clinicobiologic Neurology and Psychiatry [5]	Arranged, 10 weeks, 250 hours	100

References will be found on page 946.

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Postgraduate Continuation Courses for Practicing Physicians—Jan. 1, 1947 to July 15, 1947—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
NEUROLOGY AND PSYCHIATRY—Continued			
Tennessee State Medical Association, 4 University Center Building, Memphis, Tenn. At: County Seat towns through the State (45)	Psychiatry as Applied to the Practice of Medicine	Jan. 1, 1947-Jan. 1, 1949, 14 week course at 45 centers; 1 week in each center	10
University of Texas Medical Branch, Galveston, Tex.	Electroencephalography	By arrangement	Not given
	Electro-shock Therapy	By arrangement	Not given
	Technical Procedures of the Neurological Examination	By arrangement	Not given
NEUROSURGERY			
Duke University School of Medicine, Durham, N. C.	Neurosurgery	Arranged, 3 mo. or longer, full time	150 per qtr.
NUTRITION			
College of Medical Evangelists, 312 North Boyle Avenue, Los Angeles 33 At: White Memorial Hospital	Nutrition	Feb. 12, 19, 26, 1947, afternoons and evenings	35
New York Medical College, Flower and Fifth Avenue Hospitals, 1 East 105th St., New York	Nutrition	Arranged, 1 mo.	150
Duke University School of Medicine, Durham, N. C.	Nutrition	Arranged, 3 mo. or longer, full time	150 per qtr.
OBSTETRICS AND GYNECOLOGY			
Alabama State Health Department and Jefferson County Health Department, Birmingham, Ala. At: Slossfield Health Center	Institute for Negro Physicians	July 15-17, 1947, 3 days	$ 15
University of Alabama School of Medicine, University, Ala.	Obstetrics and Gynecology	Feb., 1947, 1 week	None
College of Medical Evangelists, 312 North Boyle Avenue, Los Angeles 33 At: White Memorial Hospital	Obstetrics and Gynecology	Jan. 6, 1947, 6 weeks, 2 days a week, part time	35
	Obstetrics and Gynecology	March 31-June 18, 1947, 6 weeks, 2 days a week, mornings	35
George Washington University School of Medicine, 1335 H St., N.W., Washington, D. C.	Intensive Postgraduate Course in Gynecology	Feb. 24-28, 1947, 1 week, full time	50
	Intensive Refresher Course in Obstetrics and Gynecology	Feb. 17-March 7, 1947, 3 weeks, full time	150
Chicago Maternity Center, 1336 S. Newberry Street, Chicago	Postgraduate Training in Obstetrics and Gynecology	July, 1947, 4 months, full time	None
Cook County Graduate School of Medicine, 427 So. Honore Street, Chicago	Personal Course in Gynecological Surgery	Jan., 1947 (Tentative) 4 weeks, part time	80
	Personal Course in Gynecological Surgery	March, 1947 (Tentative) 4 weeks, part time	80
	Personal Course in Gynecological Surgery	May, 1947 (Tentative) 4 weeks, part time	80
	Personal Course in Gynecological Surgery	July, 1947 (Tentative) 4 weeks, part time	80
	Practical and Didactic Course in Office Gynecology	Jan. 1, 1947 (Tentative) 4 weeks, part time	80
	Practical and Didactic Course in Office Gynecology	Jan. 31, 1947 (Tentative) 4 weeks, part time	80
	Practical and Didactic Course in Office Gynecology	March, 1947 (Tentative) 4 weeks, part time	80
	Practical and Didactic Course in Office Gynecology	May, 1947 (Tentative) 4 weeks, part time	80
	Practical and Didactic Course in Office Gynecology	July, 1947 (Tentative) 4 weeks, part time	80
	Obstetrics	March 3, 1947, 2 weeks, full time	150
	Obstetrics	April 28, 1947, 2 weeks, full time	150
	Obstetrics	June 2, 1947, 2 weeks, full time	150
	Operative and Office Gynecology	March 17, 1947, 2 weeks, full time	150
	Operative and Office Gynecology	April 14, 1947, 2 weeks, full time	150
	Operative and Office Gynecology	May 12, 1947, 2 weeks, full time	150
	Operative and Office Gynecology	June 16, 1947, 2 weeks, full time	150
University of Kansas School of Medicine, Kansas City, Kan. At: University of Kansas Hospitals	Obstetrics and Gynecology	April 21-25, 1947, 5 days	20 [6]
Tulane University of Louisiana School of Medicine, 1430 Tulane Avenue, New Orleans 13	Obstetrics and Gynecology	Jan. 13-18, 1947, 5½ days, full time	25
University of Maryland School of Medicine, Lombard and Greene Sts., Baltimore	Review of Gynecology, Oncology and Female Urology	Arranged, 10 weeks	125
	Review of Obstetrics and Gynecology	Jan. 15-July 1, 1947, 5½ months	150
University of Minnesota Medical School, Department of Postgraduate Education, Minneapolis 14 At: Center for Continuation Study	Obstetrics and Gynecology	To be announced, 3 days	15
	Obstetrics and Gynecology	To be announced, 6 days	25
	Obstetrics and Gynecology	To be announced, 12 days	50
Creighton University School of Medicine, 306 North 14th Street, Omaha	Obstetrics and Gynecology	Arranged, 3 months	None
Long Island College of Medicine, Joint Committee on Postgraduate Education, 1313 Bedford Avenue, Brooklyn 2 At: Cumberland Hospital	Complications of Pregnancy	April 8, 1947, 8 sessions, twice a week	20
At: Israel Zion Hospital	Gynecological Pathology	April 9, 1947, 12 sessions, once a week, part time	50
At: Jewish Hospital	Female Sex Endocrinology	April 14, 1947, 10 sessions, once a week, part time	20
At: Long Island College of Medicine	Manikin	April 15, 1947, 10 sessions, once a week, part time	20
	Prenatal Care	April 17, 1947, 8 sessions, once a week, part time	20

1. Plus $5.00 registration fee.
2. Stipend provided when needed.
3. To be announced.
4. G. I. Bill of Rights for Veterans.
5. Specialists only.
6. No fee to World War II veterans.
7. Specialists in Internal Medicine.
8. All instruments furnished.
9. Hospital administrators.
10. Registration $15.00.
11. Fellowship—State Board of Health.
12. No charge for physicians on active duty in armed forces.
13. $45.00 for 5 days.
14. Or pro rated.
20. For medical officers only.

(To be concluded next week)

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Correspondence

LEPROSY

To the Editor:—Commenting on the letter of Dr. Cristobal Manalang of San Lazaro Hospital, Manila, P. I., in THE JOURNAL, October 19, page 407, the main points of special interest which he considers are that (1) the essential cause of leprosy is a "virus" stage of Mycobacterium leprae, (2) the disease is contracted up to the age of 4 years by frequent and prolonged contact and (3) microscopically negative as well as positive cases serve to transmit the disease. He remarks that if his views are sound they should lead to revision of public health procedures in leprosy by focusing efforts on the protection of children. Dr. Manalang suggests a study of children of leprous persons in the United States, and he points to the advantage of studying the disease in this country rather than in foreign fields.

As to Dr. Manalang's views relating to the "virus" stage of M. leprae, judgment must be reserved. To one who has seen a number of persons unquestionably infected during adult life the emphasis on childhood infection seems too strong. One is prepared to consider sympathetically the view that all types of cases may be communicable, though this is contrary to the usual opinion. That the public health management of leprosy needs "humanizing," as Dr. Manalang puts it, is obvious to any serious student of the problem. Indeed, current practice, under American jurisdiction, is based too much on misinformation and too little on established facts. The problem of control must be considered for each area separately on the basis of experience; for example, measures that might be justified in areas where the disease spreads fairly freely, as Hawaii or the Philippine Islands, would be unnecessary in the greater part of the United States, where the disease shows little or no tendency to be communicable.

Of special interest to dermatologists is Dr. Manalang's assertion that the early lesions of leprosy are likely to be confused with those of lupus erythematosus, tuberculosis, syphilis or Boeck's sarcoid. While these conditions may on superficial study be mistaken for leprosy or vice versa, the laboratory tests that should always be made would speedily confirm or exclude a diagnosis of leprosy, since the conditions mentioned would be likely to be confused only with the form of leprosy that yields characteristic microscopic findings. The proposal that the subject deserves study by the Section on Dermatology and Syphilology of the American Medical Association merits friendly consideration.

G. W. MCCOY, M.D., New Orleans.

COLD PACKS FOR PREVENTION OF MUMPS ORCHITIS

To the Editor:—In reference to the communication from Novak in THE JOURNAL, October 26, page 472, suggesting that cold packs would be a protection for the testes in the orchitis of mumps, it should be pointed out that the pathologic process in "mumps orchitis" is apparently an acute hydrocele which causes secondary strangulation, edema, fibrosis and atrophy of the testis rather than a true testis inflammation.

Incision and drainage of the acute hydrocele immediately relieves the pressure on the testis and protects it from further strangulation atrophy. A series of cases treated in this manner was reported by Robert A. Burhans in the *Journal of Urology* **54**:547 (Dec.) 1945.

DAVID ROSENBLOOM, M.D., Los Angeles.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS
EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and the Examining Board in Specialties were published in THE JOURNAL, Dec. 7, page 880.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, Jan. 21-23. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, January. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

CALIFORNIA: *Examination.* Los Angeles, March 10-13. Sec., Dr. Frederick N. Scatena, 1020 N. St., Sacramento 14.

COLORADO: * Denver, Jan. 7-10. Sec., Dr. J. B. Davis, 831 Republic Bldg., Denver 2.

DELAWARE: *Examination.* Dover, Jan. 14-16. *Endorsement.* Dover, Jan. 21. Sec., Medical Council of Delaware, Dr. J. S. McDaniel, 229 S. State St., Dover.

GEORGIA: Atlanta and Augusta, June. Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

HAWAII: Honolulu, Jan. 13-16. Sec., Dr. S. E. Doolittle, 881 S. Hotel St., Honolulu 53.

IDAHO: Boise, Jan. 14. Dir., Bureau of Occupational Licenses, Miss Agnes Barnhart, 355 State Capitol Bldg., Boise.

INDIANA: *Examination.* Indianapolis, June. Exec. Sec., Board of Medical Registration and Examination, Miss Ruth V. Kirk, 627 K. of P. Bldg., Indianapolis.

KENTUCKY: *Examination.* Louisville, Dec. 16-18. Sec., State Board of Health, Dr. P. E. Blackerby, 620 S. Third St., Louisville 2.

MINNESOTA: * Minneapolis, Jan. 21-23. Sec., Dr. J. F. Du Bois, 230 Lowery Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson 113.

MISSOURI: *Examination:* Kansas City, Jan. 27-29. Exec. Sec., Department of Education, Mr. John A. Hailey, State Capitol Bldg., Jefferson City.

MONTANA: Helena, April 1-2. Sec., Dr. O. G. Klein, First National Bank Bldg., Helena.

NEBRASKA: * *Examination.* Omaha, June 1947. Dir., Bureau of Examining Board, Mr. Oscar F. Humble, State Capitol Bldg., Lincoln.

NEW HAMPSHIRE: Concord, March 13. Sec., Board of Registration in Medicine, Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: Trenton, June 17-18. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 7-8. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 27-30. Sec., Dr. Jacob L. Lochner, Education Bldg., Albany.

NORTH CAROLINA: *Examination.* Winston-Salem, Dec. 16-19 postponed. *Endorsement.* Raleigh, Jan. 16. Act. Sec., Mrs. L. McNeill, 226 Hillsboro St., Raleigh.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: * *Reciprocity.* Oklahoma City, Dec. 29-30. Sec., Dr. J. D. Osborn Jr., Frederick.

OREGON: * Portland, Jan. 22-25. Exec. Sec., Miss L. M. Conlee, 608 Failing Bldg., Portland 4.

RHODE ISLAND: * Providence, Jan. 2-3. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA:* Vermillion, Jan. 21-22. Sec., Dr. Gilbert Cottam, State Capitol Bldg., Pierre.

TENNESSEE: * Memphis, Dec. 18-19. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis 3.

TEXAS: *Examination.* Galveston, Feb. 20-22. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.

UTAH: Salt Lake City, Dec. 18-20. Asst. Dir., Department of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City 1.

VERMONT: *Examination.* Burlington, Jan. 31-Feb. 1. Sec., Board of Medical Registration, Dr. F. J. Lawliss, Richford.

WASHINGTON: *Examination.* Seattle, January 1947. Sec., Mr. Nelson Vaughn, Olympia.

WEST VIRGINIA: Charleston, Jan. 6-8. Commissioner, Public Health Council, Dr. N. H. Dyer, State Capitol, Charleston 5.

WYOMING: Cheyenne, Feb. 3. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Dec. 17. Sec., Mr. Francis A. Roy, Science Hall, University of Arizona, Tucson.

CONNECTICUT: Feb. 8. Address State Board of Healing Arts, 250 Church St., New Haven.

DISTRICT OF COLUMBIA: Washington, April 21-22. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington 1.

FLORIDA: May 31. Sec., Dr. M. W. Emmel, University of Florida, Gainesville.

IOWA: Des Moines, Jan. 14. Corresponding Sec., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines 19.

MICHIGAN: Ann Arbor and Detroit, Jan. 10-11. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing 15.

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NEBRASKA: Omaha, Jan. 14-15. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln 9.

OREGON: Portland, March 1. Sec., Board of Higher Education, Mr. C. D. Byrne, University of Oregon, Eugene.

TENNESSEE: Memphis and Nashville, Dec. 19-20. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis 3.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Physiology, Baltimore

146:637-766 (Aug.) 1946

Theoretical Study of Composition of Alveolar Air at Altitude. W. O. Fenn, H. Rahn and A. B. Otis.—p. 637.
Effect of Hemorrhage on Plasma Amino Nitrogen of Dog. D. L. Kline. —p. 654.
Effect of Infusion of Renin on Flow and Protein Content of Lymph of Anesthetized Dogs. Florence W. Haynes and Esther Hardenbergh. —p. 666.
Influence of Hepatectomy on Relative Concentrations of Protein Components of Dog Plasma as Determined by Electrophoresis. Muriel Platt Munro and Annabel Avery.—p. 673.
Effect of Intra-Arterially Injected Adrenalin on Blood Flow, Sugar Retention and Lactate Output of Leg Tissues of Anesthetized Cats. F. R. Griffith, Julia E. Lockwood and T. A. Loomis.—p. 677.
Dark Adaptation of Color Anomalous. A. Chapanis.—p. 689.
Effect of Para-Aminopropiophenone-Induced Methemoglobinemia on Oxygenation of Working Muscle in Human Subjects. J. Tepperman, O. Bodansky and B. J. Jandorf.—p. 702.
Respiratory Metabolism of Human Subjects During Prolonged Exposures to Simulated Altitudes of 8,000 and 10,000 feet. S. A. D'Angelo. —p. 710.
Pyridoxine Deficiency in Dogs as Affected by Level of Dietary Protein. Agnes Fay Morgan, Mary Groody and Helen E. Axelrod.—p. 723.
Simultaneous Determinations of Blood Volume by Co and Dye (T-1824) Under Various Conditions. W. S. Root, F. J. W. Roughton and M. I. Gregersen.—p. 739.

American Journal of Public Health, New York

36:963-1104 (Sept.) 1946

*Illumination Standards. M. A. Tinker.—p. 963.
Recent Developments in Murine Typhus Fever Control. J. S. Wiley. —p. 974.
Race Relations in Community Health Organization. P. B. Cornely. —p. 984.
Health Education Program in Puerto Rico. Alice Miller Johnson. —p. 993.
Modern Treatment of Syphilis. E. W. Thomas.—p. 1002.
*Refrigeration in Food Control Program. H. S. Adams.—p. 1007.
What Good Are Health Museums? B. Gebhard.—p. 1012.
Appraisal Forms and Sanitation Standards Used in Michigan Community Health Project. H. J. Dunsmore.—p. 1016.
Gonococcus Examinations: Comparison of Slides, Mailed Slants and Immediate Plates. Grace Eldering and Evelyn Palser.—p. 1023.
*Dangers Associated with Use of Living "Attenuated" Typhus Vaccine. J. F. Sadusk Jr. and H. Kuhlenbeck.—p. 1027.
Place of Entomologist in Public Health. T. A. Olson.—p. 1031.
Use of Chlorine Dioxide in Water Treatment. G. P. Vincent and J. F. Synan.—p. 1035.

Illumination Standards.—Tinker points out that codes of lighting have been issued by the Illumination Engineering Society either alone or jointly with the American Institute of Architects. He thinks that more satisfactory approach to hygienic lighting might be achieved by coordinating the work of engineers, physiologists and psychologists. It is obvious that visual work should not be done at critical levels of illumination. There should be an adequate margin of safety to provide for individual variation. For such visual tasks as reading good sized print (10 to 11 point) on a good quality paper, 10 to 15 foot candles should provide hygienic conditions when one's eyes are normal. For the reading of newsprint, 15 to 20 foot candles should be adequate. In situations involving the reading of handwriting and other comparable tasks, 20 to 30 foot candles seems desirable. For tasks comparable to discrimination of 6 point type there should be 30 to 40 foot candles. For the most severe tasks encountered in workday situations 40 to 50 foot candles will be found adequate. There is no valid experimental work now available that indicates a need for over 50 foot candles intensity for adequate visual discrimination. These suggestions hold for school children as well as for adults. Intensity of illumination cannot be prescribed without coordinating it with other factors such as distribution of light and brightness contrast.

Refrigeration for Food.—In a survey of 300 restaurants, Adams found that the refrigerator temperature in 26 per cent of them exceeded 50 F. While 50 F. is generally accepted as the maximum allowable temperature for the storage of many perishable foods, a temperature several degrees lower is preferable. For fresh meat a range of 35 to 40 F. is recommended, and for poultry 29 to 32 F. Food should not be stored on top of cooling units or on the drip pan below the unit, since such a practice restricts air circulation and may contribute to frosting of the unit. Refrigerator shelves should not be covered with paper, linoleum or similar material, since this causes stagnation of air, creates excessive sweating of products and increases operating expense. Fresh meat should be stored so there is a complete circulation of cool air around it. Placing large amounts of food in a single container should be avoided. Ultraviolet light in conjunction with refrigeration is used mainly as an inhibitor to microbic growth. Reduction of air borne infection and removal of objectionable odors from cold storage boxes is also claimed when ultraviolet light is used. Ultraviolet rays have little penetrating power, so that even very thin films of dirt or moisture may shield the micro-organisms from the damaging effect of the radiation. The question of rancidity must also be recognized. Butter, cream, lard and fat sausages exposed to direct radiation will become rancid and must be protected by storing in a covered container. Fats or fish likewise are adversely affected by short wavelengths of light and by ozone.

Dangers of "Attenuated" Living Typhus Vaccine.—Sadusk and Kuhlenbeck give an account of difficulties encountered by Japanese health authorities following the administration of a biliated living murine typhus vaccine. In a group of 290 persons inoculated with this vaccine, 218 (70 per cent) developed symptoms and serologic manifestations of typhus fever. There was 1 fatality. The record of the use of living typhus vaccine presents a series of frank failures. The authors stress the favorable results which have been recently obtained against epidemic typhus by the use of a killed ether extracted yolk sac vaccine.

Anesthesiology, New York

7:477-598 (Sept.) 1946

Anesthesia in Surgical Treatment of Congenital Pulmonic Stenosis. M. H. Harmel and A. Lamont.—p. 477.
Pontocaine—Dextrose—Ephedrine for Spinal Anesthesia. J. K. Potter and R. J. Whitacre.—p. 499.
Effect of Pentothal Alone and in Combination with Oxygen or Nitrous Oxide-Oxygen on Arterial Blood Gases. G. D. Barton, W. R. Wicks and H. M. Livingstone.—p. 505.
Lethal Hypothermia in Dogs of Various Ages. B. De Boer and H. E. Ederstrom.—p. 518.
*Use of Curare for Abdominal Surgery in Seriously Injured Patients. E. A. Doud and G. Shortz.—p. 522.
Question of Cerium Oxalate as Prophylactic Against Postoperative Vomiting. T. Gordh and H. Rydin.—p. 526.
Stages and Signs of Pentothal Anesthesia: Physiologic Basis. B. Etsten and H. E. Himwich.—p. 536.
Rotameter in Anesthesia. R. Foregger.—p. 549.
Regional Anesthesia by Intravenous Route (Slight Modification of Bier's Method). L. Garcia Herreros.—p. 558.

Curare for Abdominal Surgery.—The intravenous administration of curare (intocostrin) was employed by Doud and Shortz as an adjunct to anesthesia in 26 cases of severe abdominal and thoracoabdominal injuries. Ether, with the oroendotracheal absorption technic, and nitrous oxide-oxygen were the agents in all cases. No untoward effects have been observed. Doses of curare sufficiently large to produce respiratory depression or paralysis of short duration did not cause hypotension. Deaths occurring in the series could not be attributed to curare. The surgeons declared that the relaxation was excellent and that the operating time was decreased because manipulation of intraperitoneal contents was easier, exposure readily obtained and closure greatly facilitated. The element of shock present in association with severe abdominal wounds does not appear to contraindicate the use of curare as an anesthesia adjunct.

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Annals of Internal Medicine, Lancaster, Pa.

25:403-584 (Sept.) 1946

*Evaluation of Several Methods for Treating Graves' Disease Available Today. J. H. Means.—p. 403.
Penicillin Therapy Alone in Neurosyphilis: Analysis of Clinical Results. G. D. Gammon, J. H. Stokes and others.—p. 412.
Evaluation of Sulfonamide Mixtures and Various Adjuvants for Control of Sulfonamide Crystalluria. H. F. Flippin, J. G. Reinhold, with technical assistance of Lillian Pollack and Elaine Clausen.—p. 433.
*Immunization Against Influenza. J. E. Salk and T. Francis Jr.—p. 443.
Hepatic Insufficiency: I. Pathophysiology and Clinical Aspects. S. S. Lichtman.—p. 453.
Colorado Tick Fever. L. Florio, E. R. Mugrage and Mabel O. Stewart. —p. 466.
Association of Acute Pulmonary Lesions with Infections of Throat. Commission on Acute Respiratory Diseases.—p. 473.
Carbon Tetrachloride Poisoning: Report of 1 Case with Necropsy and 1 Nonfatal Case, with Clinical Laboratory Studies. W. B. Martin, L. H. Dyke Jr., F. L. Coddington and A. M. Snell.—p. 488.
Reiter's Disease with Prolonged Auriculoventricular Conduction. W. Feiring.—p. 498.
*Intoxication Resulting from Administration of Massive Doses of Vitamin D, with Report of 5 Cases. G. W. Covey and H. H. Whitlock. —p. 508.

Methods for Treating Hyperthyroidism.—Means believes that the antithyroid drugs such as thiouracil when used in combination with iodine in the preparation of patients with hyperthyroidism for thyroidectomy provide a more complete preparation than has been available heretofore. As between treatment of hyperthyroidism by thyroidectomy after preparation with an antithyroid drug in combination with iodine, and treatment by prolonged use of an antithyroid drug alone, the author believes that the scales still tip in favor of surgery. Treatment with radioactive iodine is an effective way of producing a remission in the thyrotoxicosis of hyperthyroidism, but a final evaluation of how it compares with other modes of treatment must await observation of more cases and over a longer period of time, particularly with respect to late untoward side-effects, malignancy and renal damage.

Immunization Against Influenza.—Salk and Francis employed a vaccine which consisted of a suspension of formaldehyde inactivated influenza viruses and contained representative strains of both type A and type B. The culture medium for the virus was the chick embryo, and the extraembryonic fluids constituted the immediate source. During the epidemic of influenza A that occurred throughout the United States in the winter of 1943-1944, 12,500 students in the specialized training program were involved in studies conducted uniformly but independently by members of the Commission on Influenza in six investigating groups in different parts of the country. The estimate that vaccination was 75 per cent effective assumes that the attack rate in the control half of the population under study was not influenced by the presence of vaccinated persons but was the expected rate had vaccination not been done. Observations which have a bearing on this point suggest that the assumption may be incorrect. The general opinion has been that the duration of the effectiveness of influenza is a matter of weeks or months, but the authors think that such statements have been based on questionable evidence or have been made without due consideration of all of the factors involved. From recently reported studies, evidence is available to support the contention that the duration of effectiveness of influenza vaccination is considerably longer than a few months when vaccine of suitable potency is employed. Reactions to influenza vaccine correspond in severity and character to reactions following the administration of typhoid vaccine. Although incontrovertible evidence is now available that the resistance of man to infection by the viruses of influenza A and B can be enhanced, it is also evident that the problem of controlling epidemics of influenza by means of immunization cannot be approached only from the point of view of affording individual protection.

Intoxication from Massive Doses of Vitamin D.—Covey and Whitlock state that vitamin D in massive doses is a powerful and dangerous drug which should be used with caution and that there are definite contraindications to its use. It mobilizes calcium from the trabeculae of the bones and thus raises the blood calcium level. It often produces cellular degeneration in various organs of the body, and this is most obvious in the kidney. The degenerated cells become the repository for calcium. The fat tissue of the body is rapidly burned up. Nitrogen may accumulate in the blood, presumably because of inability of the damaged kidney to excrete it. It is also apparent that mild intoxication with this drug is probably harmless unless it is permitted to continue over a long time and that complete restitution of the injured tissues usually takes place. In 4 of the 5 patients observed by the authors, ranging in age from 29 to 68 years, vitamin D was taken in dosage larger than is considered safe, namely 150,000 units per day. Two of the 5 patients were victims of arteriosclerosis and hypertension, conditions which have been said to contraindicate the use of this drug. Two patients increased the dosage voluntarily much beyond the amount ordered by the physician. The mental status of the first patient, while not obviously psychotic, was known to have deteriorated in comparison with previous observations. It is possible that psychic disorders, especially in the aged, should be regarded as a contraindication to the use of this substance in massive dosage. The most common symptoms were nausea, vomiting and headache. Associated with these symptoms there was a group of findings indicating renal injury. The authors conclude that the use of this substance should always be carefully supervised.

Archives of Internal Medicine, Chicago

78:255-368 (Sept.) 1946

Tropical Ulcers and Cutaneous Diphtheria. A. A. Liebow, P. D. MacLean, J. H. Bumstead and L. G. Welt.—p. 255.
*Methemoglobinemia: Treatment with Ascorbic Acid. M. Carnrick, B. D. Polis and T. Klein.—p. 296.
Löffler's Syndrome Associated with Creeping Eruption (Cutaneous Helminthiasis): Report of 26 Cases. D. O. Wright and E. M. Gold. —p. 303.
*Treatment of Gummatous Hepatic Syphilis with Penicillin: Report of 2 Cases H. A. Tucker and D. D. Dexter.—p. 313.
Gastroenterology: Review of Literature from July 1944 to June 1945. W. L. Palmer, W. E. Ricketts and S. N. Maimon.—p. 323.

Methemoglobinemia: Treatment with Ascorbic Acid.—Carnrick and his associates say that in the absence of cardiac or pulmonary disease further study of the blood to establish or exclude the presence of methemoglobin is of considerable importance. They recently encountered 2 patients presenting cyanosis as an important symptom. In 1 the disease is of unusual interest in that a spontaneous formation of methemoglobin was apparently the cause of the cyanosis. In the other patient sodium nitrite therapy was the cause of the cyanosis. Methemoglobinemia is commonly accompanied not only with cyanosis but also with disturbances in gastrointestinal function; frequently diarrhea has been noted. In 1 of the patients here presented the combination of cyanosis and gastrointestinal symptoms was prominent. In both patients methemoglobinemia was suspected and confirmed by laboratory studies. Of particular importance in both cases was the striking response of the cyanosis to treatment with ascorbic acid, with concomitant alleviation of all clinical symptoms. The first patient was given 500 mg. of ascorbic acid daily by mouth in divided doses for three days. In the second patient 500 mg. of ascorbic acid was given intravenously. Within four hours there was a noticeable decrease in the amount of cyanosis. An additional 500 mg. of ascorbic acid was injected intravenously during the remainder of the day in three divided doses. Fifty-six hours after the initial therapy the hemoglobin level had fallen from 3.9 Gm. to 0.4 Gm. per hundred cubic centimeters. Treatment of methemoglobinemia has been undertaken in the past by the use of intravenously administered methylthionine chloride, but the authors think that ascorbic acid is more desirable for this purpose.

Penicillin in Hepatic Syphilis.—According to Tucker and Dexter active late syphilis of the liver is a condition rarely demonstrated clinically. The initial and essential lesion is the gumma. Two methods are available for proving the presence of active hepatic gummas. The first and more reliable method is to make a biopsy, a procedure not without risk. The second method is to employ a therapeutic test. In the 2 cases reported here, penicillin was used. The patients received 920,000 and 3,200,000 Oxford units respectively of commercial sodium penicillin intramuscularly, with dramatic alleviation of acute symptoms and sustained objective and subjective improvement over observation periods of six hundred and eighty-six and four hundred and ninety-one days. These results show that visceral

gummas heal under treatment with commercial penicillin mixtures at least as well as they do under other forms of antisyphilitic treatment. The apparently nontoxic properties of penicillin recommend it particularly in cases in which disease of the liver is present. In the second of these 2 cases the diagnosis was substantiated also by biopsy.

Archives of Surgery, Chicago

53:247-358 (Sept.) 1946

*Pathologic Intervertebral Disk and Its Consequences: Cause and Treatment of Chronic Pain Low in Back and Subject of Herniating Intervertebral Disk. O. R. Hyndman.—p. 247.
Acute Superior Mesenteric Artery Thrombosis: Recovery Following Extensive Resection of Small and Large Intestines. H. W. Meyer. —p. 298.
Zephiran Chloride for Preoperative Preparation of Hands. D. L. Lovell. —p. 304.
Repair of Defects of Skull, with Special Reference to Periorbital Structures and Frontal Sinus. O. A. Turner.—p. 312.
Chemosurgical Treatment of Cancer of Nose: Microscopically Controlled Method. F. E. Mohs.—p. 327.
New Method of Leg Exercises. J. K. Narat and A. F. Cipolla.—p. 345.
Reaction of Tissue to and Fate of Oxidized Cellulose in Peritoneal Cavity of Dog. F. J. Burns.—p. 348.
Nontraumatic Spontaneous Rupture of Spleen. I. Silverman and A. P. Randazzo.—p. 355.

Chronic Back Pain and Herniating Intervertebral Disk.—Hyndman presents evidence that degeneration and disintegration of intervertebral disk in the low lumbar region is the predominant cause of chronic pain low in the back. Herniation and rupture of a disk is an advanced stage of degeneration and is associated with the syndrome of compression of a nerve root. The process of degeneration of the nucleus pulposus and annulus fibrosus is a prerequisite to herniation. Whatever role trauma may play, it is only an accessory one. The syndrome of chronic pain low in the back is due to a weakened lumbar or lumbosacral joint. The syndrome of radiating pain in sciatic distribution is due to compression of a nerve root. These two syndromes are separate entities. They are due to different aspects of the same pathologic process and hence may exist independently or combined. Treatment of the degenerating disk consists in removal of the pathologic tissue. The result is contingent on the development of a new fibrocartilaginous disk that serves to fuse the adjacent vertebrae into a mechanical unit. There are a number of different types of herniation.

Blood, New York

1:367-458 (Sept.) 1946

Further Observations on Effect of Benzene on Strain of Myeloid Chloroleukemia in Mice and on Changes Produced in Leukemic Cells by the Chemical. C. M. Flory, I. D. Steinhardt and J. Furth. —p. 367.
Cellular Changes Produced by Extracts of Human Organs. L. A. Erf, D. L. Turner and F. R. Miller.—p. 379.
Monocytic Leukemia and Tuberculosis. E. L. Heller and C. H. Hiles. —p. 387.
Plasma Cell Leukemia. W. T. Moss and L. V. Ackerman.—p. 396.
Morphologic Examination of Blood and Sternal Marrow of 9 Patients Treated with Thiouracil. C. J. Gessler.—p. 407.
Sternal Marrow Studies in Thyrotoxicosis Treated with Thiouracil and Review of Literature Regarding Thiouracil Effects on Blood. Stella H. Sikkema, Ethel W. Thewlis and O. O. Meyer.—p. 411.
Effect of Thiouracil on Leukemia. L. R. Limarzi, R. J. Kulasavage and C. L. Pirani.—p. 426.

Cancer Research, Baltimore

6:529-592 (Oct.) 1946

Transplantability and Presence of Virus in Spontaneous Sarcomas and Fibromas of Chickens in Relation to Age of Tumor Bearing Animal. F. D. Reynals.—p. 529.
Study of Five Transplantable Chicken Sarcomas Induced by Viruses. F. Duran-Reynals and E. W. Shrigley.—p. 535.
Transplantability of Lymphoid Tumors, Embryonal Nephromas and Carcinomas of Chickens. F. Duran-Reynals.—p. 545.
Some Effects of Aromatic Hydrocarbons on Sulfur Metabolism and Tumor Induction in Mice. H. G. Crabtree.—p. 553.
Stimulation and Retardation of Neoplastic Growth by Sulfhydryl Compounds. A. Brunschwig, J. Arnold and J. Edgcomb.—p. 560.
Effect of Fresh Milk on Production of Hepatic Tumors in Rats by Dimethylaminoazobenzene. Cornelia Hoch-Ligeti.—p. 563.
Water Content in Epidermis of Mice Undergoing Carcinogenesis by Methylcholanthrene. V. Suntzeff and C. Carruthers.—p. 574.
Tubular Adenomas and Testis-like Tubules of Ovaries of Aged Rats. E. T. Engle.—p. 578.

Diseases of Chest, Chicago

12:371-514 (Sept.-Oct.) 1946

Pulmonary Coccidioidomycosis. H. E. Bass, S. I. Kooperstein, M. M. Friedman and G. H. Kastlin.—p. 371.
Lobectomy and Pneumonectomy in Pulmonary Tuberculosis. D. Carr and J. S. Harter.—p. 387.
Spontaneous Hemothorax: Discussion of Problem Based on 3 Cases. A. Bernstein, E. Klosk and A. E. Parsonnet.—p. 394.
Pulmonary Actinomycosis (Report of First Case Observed in Isthmus of Panama). C. Calero.—p. 402.
Vitamin D: Its Bactericidal Action. W. Raab.—p. 409.
Obstructing Tuberculosis of Main Bronchi: A Syndrome. W. F. Hulse. —p. 416.
Pulmonary Cavitation: Difficulty in Differential Diagnosis by X-Ray. N. Diamond.—p. 422.
*Results of Thoracoplasty (933 Cases, 1,868 Operations). R. Davison. —p. 431.
*Concurrence of Superior Pulmonary Sulcus Tumor and Pulmonary Tuberculosis. D. Bernstein.—p. 436.
Noncoagulating Intrapleural Hemorrhage Following Damage to Intercostal Vessels. W. L. Meyer.—p. 444.
Role of Tuberculosis Sanatorium in Community. H. F. Schwartz. —p. 447.

Results of Thoracoplasty.—This review includes the patients operated on by Davison at the Chicago Municipal Tuberculosis Sanatorium since 1933. In all 1,868 operations were performed on 933 patients. The 933 patients represent 7.2 per cent of admissions. In 54 patients the tuberculosis was moderately advanced and in 879 it was far advanced. There were 57 operative deaths. This represents a mortality of 6.4 per cent. A recent review of 888 cases revealed that 488, or 55 per cent, were apparently arrested. Some were improved and had negative sputum, but others had positive sputum although they were improved. Some were unimproved and had a poor prognosis. The author concludes that the results of thoracoplasty are good when one takes into consideration the advanced stage of tuberculosis at which it is usually performed. Soon there may be a preparation available which will render thoracoplasty less frequently necessary. The most promising at present is streptomycin.

Superior Pulmonary Sulcus Tumor and Pulmonary Tuberculosis.—Bernstein presents the history of a patient with active pulmonary tuberculosis who developed Pancoast's syndrome. This is the second known instance of the concurrence of superior pulmonary sulcus tumor and pulmonary tuberculosis. In the case described by Fried in 1935 the diagnosis of Pancoast's syndrome was suspected clinically and the tumor found at necropsy. Bernstein observed his patient earlier in the course of the disease, established the diagnosis ante mortem, instituted radiation therapy and subsequently confirmed the clinical finding at necropsy. The case is reported because of its rarity and its many interesting aspects. The author concludes that the presence of pulmonary tuberculosis does not preclude the possibility of the development of cancer.

Geriatrics, Minneapolis

1:341-404 (Sept.-Oct.) 1946

Special Problems of Poor Surgical Risks Among the Aged. W. B. Kountz and L. H. Jorstad.—p. 341.
Diet in Older People. W. M. Johnson.—p. 348.
Ambulatory Illness in Older Persons. M. W. Thewlis.—p. 353.
Mental Hygiene of Aging. C. L. Williams.—p. 361.
Dermatitis in Aged. S. Epstein.—p. 369.
Mortality and Life Expectancy in United States Since 1900. W. S. Groom.—p. 384.
Old Age in Alabama. B. F. Austin.—p. 391.

Indiana State Medical Assn. Journal, Indianapolis

39:385-424 (Aug.) 1946

Anterior Poliomyelitis. R. O. Ritter.—p. 385.
Evolution of Treatment of Pilonidal Cysts and Sinuses. R. L. Clark. —p. 387.
Surgical Treatment of Undescended Testicle. R. W. Lamb.—p. 392.
Clinical Observations on Use of Penicillin. H. D. Pyle.—p. 395.
Mesenteric Cysts. P. B. Arbogast.—p. 399.
The Tonsil Stump and Its Removal. C. B. Sputh Jr. and C. B. Sputh Sr.—p. 401.
Mental Hospital of the Future. M. F. Daubenheyer.—p. 404.

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Journal of Lab. and Clinical Medicine, St. Louis

31:939-1052 (Sept.) 1946

Experimental Production of Generalized Arteritis and Periarteritis (Periarteritis Nodosa). H. C. Hopps and R. W. Wissler.—p. 939.
Paracolon Bacilli and Their Relation to Urinary Tract Infections. Isabelle G. Schaub.—p. 958.
*Conjoined Action of Penicillin and Bacteriophages. W. J. MacNeal, Louise Filak and Anne Blevins.—p. 974.
Interpretation of Weil-Felix Agglutination Test in Rocky Mountain Spotted Fever. H. Plotz.—p. 982.
Sulfonamides and Dark Adaptation. D. Slaughter.—p. 987.
Liver Function Tests in Neurosyphilitic Patients with Induced Vivax Malaria of Pacific and Mediterranean Origin. S. W. Lippincott, A. Marble, L. D. Ellerbrook and others.—p. 991.
Studies of Pancreatic Function: III. Effect of Ligation of Pancreatic Ducts on Amylase and Lipidase Content of Blood. N. P. Goldstein, M. Jacobson, I. R. Telford and J. H. Roe.—p. 999.
Production and Course of Alloxan Diabetes in Rat. A. Lazarow and S. L. Palay.—p. 1004.
Use of Heparin When Performing Exchange Blood Transfusions in Newborn Infants. A. S. Wiener and I. B. Wexler.—p. 1016.
Permeability of Human Placenta to Isoantibodies. A. S. Wiener and Eve B. Sonn.—p. 1020.
Quantitative Determination of Pepsin-like Substance in Urine of Normal Individuals and of Patients with Pernicious Anemia. Edith B. Farnsworth, E. Speer and H. L. Alt.—p. 1025.
Hemochromatosis: Review of Literature and Presentation of Case Without Pigmentation or Diabetes. C. Chesner.—p. 1029.

Conjoined Action of Penicillin and Bacteriophages.—Himmelweit, working in the laboratory of Sir Alexander Fleming at St. Mary's Hospital, London, observed that a strain of staphylococcus moderately resistant to both penicillin and bacteriophage became much more susceptible to destruction when exposed to the action of these two biologic agents in combination. Repetition of Himmelweit's experiments in the laboratory of MacNeal and his associates, using their own bacteriophages and cultures obtained from septic patients in their own series, has resulted in confirmation of his observations. Penicillin and the bacteriophages are not antagonistic to each other and in many instances exert a synergistic effect on the bacterial culture in the test tube. This combined action may be designated as a potentiating, conjoined or synergistic effect. This action is also manifest in the clinical use of these agents in treating otherwise malignant infections, particularly those due to staphylococci, colon bacilli and selected members of the streptococcus group. Severe types of infection with staphylococcus, such as chronic osteomyelitis, facial carbuncle and staphylococcic endocarditis, have responded to combined therapeutic use of penicillin and bacteriophages. Intestinal perforation associated with general peritonitis and bacteremia has been successfully treated with coli bacteriophage and penicillin. Bacterial endocarditis due to streptococci relatively resistant to penicillin has responded favorably to treatment with penicillin and suitable streptococcus bacteriophage.

Journal of Neurosurgery, Springfield, Ill.

3:359-460 (Sept.) 1946

*Radical Surgery and Penicillin in Brain Abscess: Method of Treatment in One Stage, with Special Reference to Cure of 3 Thoracogenic Cases. J. LeBeau.—p. 359.
Guides for Nerve Regeneration Across Gaps. P. Weiss and A. Cecil Taylor.—p. 375.
Observations on Encephalographic Findings in Cerebral Trauma. C. E. Troland, D. H. Baxter and R. Schatzki.—p. 390.
Separation at Suture Site as Cause of Failure in Regeneration of Peripheral Nerves. B. B. Whitcomb.—p. 399.
*Cortical Localization by Electroencephalography: Value of Quantitative and Statistical Analysis of Homologous Recordings Obtained Simultaneously. R. B. Aird and Sylvia C. Bowditch.—p. 407.
Anterior Rhizotomy: Accurate Identification of Motor Roots at Lower End of Spinal Cord. I. B. MacDonald, K. G. McKenzie and E. H. Botterell.—p. 421.
Hydrocephalus: Contribution Related to Treatment. O. R. Hyndman.—p. 426.

Radical Surgery and Penicillin in Brain Abscess.—LeBeau of the Neurosurgical Clinic of the Faculty of Medicine in Paris thinks that, because of penicillin, more radical operations can be undertaken for abscesses which otherwise could not have been cured. He advocates complete extirpation of the abscess, whether acute or chronic, single or multiple, even though this may mean opening up a communication between the abscess and the ventricle. In three operations before penicillin became available, complete extirpation could not be carried out and there were no survivals. In the next 14 cases (13 with penicillin and 1 without) complete and rapid cure was achieved. Ten of these 14 cases showed a serious form of abscess, including 3 which were metastatic from the lungs. The author has adopted the complete extirpation of the abscess in one stage by employing the method described by Clovis Vincent. He feels that with the use of penicillin brain abscesses should be dealt with like brain tumors.

Cortical Localization by Electroencephalography.—A modified electroencephalographic technic based on the quantitative and statistical analysis of homologous recordings obtained simultaneously has been investigated for its cortical localizing value by Aird and Bowditch. The principle involved is identical with that employed in the neurologic examination in which focal abnormal findings on one side are checked against the normal side as a control. This technic has been employed in 1,200 examinations. Definite cortical localizations were obtained in approximately one third of this abnormal group which gave a high degree of correlation with the clinical findings. Ninety per cent of the remainder had convulsive states or other conditions in which focal signs and symptoms or neurologic findings of localizing value were not obtained. In 248 patients of this group subjected to pneumoencephalography an all over correlation of 81 per cent was observed between the x-ray findings and those of the electroencephalogram obtained by means of the technic of homologous recordings. In 85 proved cortical lesions an electroencephalographic correlation of 95 per cent was obtained. It is estimated that electroencephalographic localization of lesions of a less gross character was made in approximately 20 per cent of the entire group, which correlated well with the clinical and pneumoencephalographic findings and which would not have been detected by other technics. The technic appears to be well justified when used for purposes of localization.

Journal of Pediatrics, St. Louis

29:269-416 (Sept.) 1946

Oral Manifestations of Congenital Heart Disease: Preliminary Report. A. Kaner, P. K. Losch and H. Green.—p. 269.
Use of Sulfadiazine-Sulfathiazole Mixture in Treatment of Children. D. Lehr, L. Slobody and W. Greenberg.—p. 275.
*To What Extent Does Fluorine Ingestion Lessen Tooth Decay? J. D. Boyd and V. D. Cheyne.—p. 286.
*Wilms' Tumor: Review of 16 Cases. R. M. Nesbit and F. M. Adams.—p. 295.
Developmental Graph for First Year of Life. C. A. Aldrich and Mildred A. Norval.—p. 304.
"Virus Pneumonia." E. C. Curnen.—p. 309.
Growth of Children with Diabetes Mellitus in Relationship to Level of Control of Disease. R. L. Jackson and Helen G. Kelly.—p. 316.
Hypoxia Tolerance Test of Heart in Children. E. Mannheimer.—p. 329.
Stramonium Poisoning: Diagnostic Problem with Psychiatric Implications. Lenore M. Sportsman.—p. 345.
Attempts to Adapt Murine Poliomyelitis Virus to Chick. P. Brutsaert, C. W. Jungeblut and Alice Knox.—p. 350.
Newer Agents in Treatment of Epilepsy. W. G. Lennox.—p. 356.
*Immunization Against Whooping Cough: Clinical Study. D. Lapointe.—p. 363.
Idiopathic Lipemia. Bertha M. Levy.—p. 367.
Practical Device to Hold Nursing Bottle During Bottle Feeding. H. W. Seiger.—p. 369.

Fluorine Ingestion and Tooth Decay.—Boyd and Cheyne think that certain communities in Iowa provide favorable facilities for the study of the effect of fluorine ingestion on tooth decay, since numerous wells in the state contain notable amounts of fluoride. During the summer of 1944 the authors conducted dental surveys in a region of endemic fluorosis and in three state controlled custodial institutions for children. The population studied was limited to subjects 13 years old or older. The dental findings have been analyzed not only in terms of place of residence and the regional content of fluoride in the domestic water supplies but also on the basis of whether or not mottling of enamel was evident. Dental data have been expressed in terms of the number of surfaces of permanent teeth which have been affected by decay. The data from this study support the thesis that the incidence of dental caries is lessened in areas of endemic fluorosis. The findings differ sharply from several reported studies in their quantitative aspects. The authors found caries of some degree in almost every subject; in many children with mottled enamel and with prolonged fluoride ingestion the incidence of carious tooth surfaces was high. Further, there was no evidence to indicate that the cur-

rent consumption of water containing submottling amounts of fluoride had lessened the progress of caries in children whose enamel was free from mottling. There is no need to conclude from studies thus far reported that teeth undergo decay primarily because of inadequacy of fluoride ingestion or because of lack of fluorine in the physicochemical structure of the tooth. Fluorinization remains a pharmacologic, not a physiologic, method for the control of caries. These points should be borne in mind in the conduct of fluorine studies. The ultimate answer to caries control probably will lie in the furtherance of innate physiologic protective agencies rather than through pharmacologic procedures.

Wilms's Tumor.—Nesbit and Adams state that the Wilms tumor, adenomyofibrosarcoma or embryonal mixed tumor of the kidney, is the most common renal neoplasm of childhood. Previous reports on this condition give a rather poor prognosis, but half of the patients under review are still living. The 16 patients were treated at the University of Michigan Hospital during the nine year period between 1934 and 1943. Twelve of the patients had nephrectomy and 7 of these are alive three and one-half to eleven and one-half years postoperatively, a survival rate of 58.4 per cent. Two of the nephrectomized patients who had retroperitoneal infiltration with neoplasm and were given postoperative irradiation have survived four and eleven years without clinical evidences of recurrence. One child considered inoperable because of questionable chest metastases was treated by x-rays alone. She has survived ten years and today appears well. The authors believe that among the 8 living patients in the present series 3 owe their survival to irradiation and are therefore led to the conclusion that postoperative irradiation of all patients is indicated.

Immunization Against Whooping Cough.—Lapointe reviews the various types of vaccines that have been employed against whooping cough and says that Strean produced a vaccine which contained 15 billion organisms per cubic centimeter combined with 150 provisional units of pertussis endotoxoid. This combined vaccine has been under clinical trial at La Creche St. Vincent de Paul since 1942. It causes the same local and general reactions encountered with the use of the bacterial type of Sauer. La Creche houses 650 children whose ages range from birth to 4 years. The children are kept in dormitories in groups of 36. The dressing rooms and playrooms are common quarters, so that the children come in close contact. Owing to crowded facilities, isolation is impossible in the event of contagious diseases. Since 1942, 150 children have been vaccinated against whooping cough every year. All received three injections of 2 cc. at one month intervals. Because some of the children were adopted and some died, there remained only 100 vaccinated in a total enrolment of 650 at the onset of an outbreak of whooping cough on July 1, 1945. The immunized children were exposed to pertussis for a longer period than is possible in a family and to much more massive infection. In spite of these unfavorable conditions, not more than 10 per cent of the immunized children contracted pertussis and none had complications or died. Of the 550 controls 450 became ill with whooping cough and 6 developed bronchopneumonia, of whom 3 died, and 2 died of mediastinal emphysema.

New England Journal of Medicine, Boston

235:285-314 (Aug. 29) 1946

*Treatment of Subacute Bacterial Endocarditis with Penicillin in Peanut Oil and Beeswax. A. J. Geiger and Jessamine R. Goerner.—p. 285.
Statistics of Diabetes. H. H. Marks.—p. 289.
Anesthesia for Radical Mastectomy with Intravenous Pentothal Sodium and Intercostal Nerve Block. J. C. McCann.—p. 295.
Active Immunization. G. Edsall.—p. 299.
Acute and Chronic Cholecystitis, with Hydrops, Producing Partial Obstruction of Cecum.—p. 305.
Strangulated Small Intestine Due to an Adhesive Band.—p. 307.

Penicillin in Peanut Oil and Beeswax in Endocarditis.—Geiger and Goerner point out that the necessity for prolonged and uninterrupted parenteral treatment in endocarditis has imposed a considerable task on the attendants and has demanded fortitude from the patients, who must either submit to intramuscular injections night and day or tolerate continuous infusion for weeks or months. These difficulties could be eliminated if sustained serum penicillin levels were attainable by the infrequent injection of massive deposits of penicillin in a slowly absorbable form. In 2 cases of subacute bacterial endocarditis due to Streptococcus viridans the authors effected apparent cure with one or two daily injections of massive doses of penicillin in a mixture of peanut oil and beeswax. In another case which had proved refractory to cure after ten months' treatment with water soluble penicillin given parenterally an afebrile and asymptomatic state with sterility of the blood was maintained with a single daily injection of penicillin in oil and beeswax. Positive blood cultures, however, were obtained whenever this treatment was discontinued. It is believed that this patient can be kept indefinitely in remission by this simple treatment. Satisfactory serum penicillin concentrations were present for twelve hours and often for twenty-four hours following a single injection of 300,000 to 600,000 units of penicillin in oil and beeswax.

235:315-346 (Sept. 5) 1946

*Pulmonary Tuberculosis in Harvard Medical Students. H. P. Brean and L. W. Kane.—p. 315.
Dyspepsia, Ulcer and Gastric Cancer. T. J. Anglem.—p. 322.
Vaginal Ureteral Orifices. W. M. Flagg.—p. 325.
Use of Streptomycin in Colon Bacillus Peritonitis: Report of Case. S. R. Muellner and A. Rutenberg.—p. 327.
Active Immunization. G. Edsall.—p. 328.
Papillary Carcinoma of Ureter.—p. 337.
Dermoid Cyst of Ovary, with Torsion and Infarction.—p. 340.

Pulmonary Tuberculosis in Medical Students.—Brean and Kane assert that tuberculous infection of the lung remains the most serious medical problem that confronts the medical student. They review the material on pulmonary tuberculosis that has accumulated in the records of the health office at Harvard Medical School during the last twenty-three years. The incidence of significant active adult type pulmonary tuberculosis was 2.2 per cent. Although the number of cases of pulmonary tuberculosis discovered in the last two years of the medical school course was four times as great as the number developing in the first two years, the incidence of acquisition of tuberculous infection was about the same (12 or 13 per cent annually) for each academic year. This constant annual attack rate suggests that factors other than opportunity for infection are responsible for the fourfold increase in cases of pulmonary tuberculosis during the term of clinical training. The duration of disability caused by the pulmonary lesion was closely correlated with the severity of the lesion at the time of its discovery. Lesions detected by the appearance of symptoms were of greater severity and carried a far greater period of disability than those discovered by routine methods. The adoption of a program in which surveys are made at intervals more frequent than once a year led to the elimination of almost all symptom detected cases and of all major lesions. It is the belief of the authors that a semiannual examination represents the maximum interval for routine reexamination by x-ray or by tuberculin tests not only for medical students but also for nurses and interns.

New Orleans Medical and Surgical Journal

99:95-142 (Sept.) 1946

The Physician as a World Citizen. R. B. Allen.—p. 95.
Mixed Tumors of Parotid Gland. J. D. Martin.—p. 99.
Some Common Errors in Fracture Treatment. L. K. Loomis.—p. 102.

Symposium on Sodium and Water Balance

Distribution of Potassium and Sodium in Body. F. N. Martin Jr.—p. 103.
Bound Water. L. M. N. Bach.—p. 107.
Sodium and Potassium in Relation to Action of Diuretics. R. G. Smith.—p. 110.
Role of Adrenal Gland in Sodium and Water Exchange. A. Segaloff.—p. 113.
Antidiuretic Hormone. T. Findley.—p. 115.
Diuretic Hormone. W. Parson.—p. 118.
Turnover of Water and Salt. P. B. Reaser and G. E. Burch.—p. 122.
Water and Sodium Balance in Congestive Heart Failure. G. Burch and P. Reaser.—p. 124.

Occupational Medicine, Chicago

2:93-182 (Aug.) 1946

What Industry Expects of Medicine. H. Strong.—p. 93.
Noxious Vapors in Aircraft Cabins. H. Speert.—p. 101.
Personality Components in Employment Problems. E. K. Clark and S. G. Law.—p. 116.
Controlled Nuclear Energy: Its Attendant Hazards and Benefits. A. H. Dowdy.—p. 126.
Atomic Disintegration. J. W. Kennedy.—p. 132.

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Ohio State Medical Journal, Columbus

42:889-992 (Sept.) 1946

Surgical Treatment of Hypertension. E. W. Shannon.—p. 921.
Orthostatic Hypotension: Its Occurrence in Dermatology. J. D. Walters.—p. 925.
Simultaneous Traumatic Dislocation of Both Right Hip and Right Knee Joint: Case Report. P. C. Doran.—p. 928.
165 Acute Combined Wounds of Thorax and Abdomen. W. H. Falor, H. W. Jones and C. B. Burbank.—p. 931.
Demonstration of Tubercle Bacilli—Survey of Methods Used in Ohio and Recommended Procedures. R. J. Ritterhoff and Loretta Hurrell. —p. 940.

Psychoanalytic Quarterly, Albany, N. Y.

15:279-418 (July) 1946

Some Remarks on Freud's Place in History of Science. O. Fenichel. —p. 279.
Masochism in Paranoia. R. C. Bak.—p. 285.
Psychoanalytic Study of Ulcerative Colitis in Children. Melitta Sperling. —p. 302.
Case of Sterility. Edith Jacobson.—p. 330.
Depression Which Recurred Annually. G. Frumkes.—p. 351.

Public Health Reports, Washington, D. C.

61:1231-1258 (Aug. 23) 1946

*Tularemic Pneumonia: Treatment with Streptomycin. R. L. Peterson and R. R. Parker.—p. 1231.
Winter Survival of Aedes Aegypti (L.) in Houston, Texas. S. P. Hatchett.—p. 1234.
Precipitin Technic for Determining Mosquito Blood Meals. E. H. Arnold, S. W. Simmons and Dorothy G. Fawcett.—p. 1244.

61:1259-1294 (Aug. 30) 1946

World Health Organization. From the Office of International Health Relations, U. S. Public Health Service.—p. 1259.
Charter for World Health. T. Parran.—p. 1265.
Constitution of World Health Organization.—p. 1268.

61:1295-1338 (Sept. 6) 1946

What Is Early Tuberculosis? H. E. Hilleboe.—p. 1295.
BCG Vaccination in Denmark. J. Holm.—p. 1298.
Control of Bovine Tuberculosis in the United States. From the Office of Tuberculosis Control Division, U. S. Public Health Service. —p. 1315.

Streptomycin in Tularemic Pneumonia.—Peterson and Parker report that a man aged 29, who was an employee of the Rocky Mountain Laboratory, became suddenly ill on Feb. 23, 1946 with a chill followed by fever, sweating and headache. Cough and pleuritic pain appeared on the fourth day. On March 1 the patient was hospitalized. X-ray examination of the chest showed diffuse infiltration of the lower lobe of the left lung. Fifty thousand units of penicillin was given intramuscularly, followed by 25,000 units every three hours, but the course remained febrile. On March 6 the diagnosis of tularemic pneumonia was established by laboratory tests. Penicillin was discontinued and streptomycin hydrochloride was administered intramuscularly, 50,000 units every three hours for eighteen doses. This exhausted the available supply. Three days later a supply of streptomycin sulfate was received. On March 11 streptomycin therapy was resumed. The patient was able to sit up on March 12 and was discharged from the hospital on March 15. The patient received 0.9 million units during the first course of treatment and 1 million during the second course, a total of 1.9 million units of streptomycin. It is doubtful whether the second series was necessary. The patient had been afebrile for three days when the second course was started.

Rhode Island Medical Journal, Providence

29:641-724 (Sept.) 1946

Seven Years' Experience in Convalescent Care of Rheumatic Fever. J. P. Hubbard, L. A. Sieracki and Isabelle Jordan.—p. 655.
Hemangiomas: Should Treatment be Expectant or Active? F. Ronchese. —p. 658.
Diethylstilbestrol in Prevention of Orchitis Following Mumps. J. Savran.—p. 662.
Waterhouse-Friderichsen Syndrome. L. Abramson and F. Mayner. —p. 663.
Expanded Federal-State Vocational Rehabilitation Program. C. L. Newberry.—p. 685.

South Carolina Medical Assn. Journal, Florence

42:241-266 (Sept.) 1946

Sympathetic Nerve Interruption in Treatment of Organic Obstructive Vascular Disease. H. G. Smithy.—p. 241.
Pyelocystostomy in Infant. R. A. Way, G. D. Johnson and F. T. Wallace.—p. 246.
Some Technical Considerations in Thyroidectomy. F. T. Wallace.—p. 248.

42:267-294 (Oct.) 1946

Some Common Proctologic Conditions of Childhood. L. J. Hirschman. —p. 267.
Medical Treatment of Gallbladder Disease. J. A. Boone.—p. 272.
Public Health, the Politician and the Doctor. L. S. Goin.—p. 274.

Surgery, St. Louis

20:315-444 (Sept.) 1946

Treatment of Extremities Following Sudden Failure of Circulation. G. Murray, J. S. Simpson and N. A. Watters.—p. 315.
*Gangrene Following Fracture Treated with Heparin, Papaverine and Intermittent Venous Occlusion: Report of Case; Reasons for Using Heparin. J. McLean and A. B. Johnson.—p. 324.
Hydronephrosis: IV. Surgical Treatment. F. Hinman.—p. 337.
*Method for Chemical Production of Prolonged Sympathetic Paralysis: Report of Its Use in 2 Patients with Causalgia. T. B. Rasmussen and A. A. Alessi.—p. 360.
Tenon and Mortise Grafts for Bridging Metacarpal Defects Due to Gunshot Wounds. H. D. Morris.—p. 364.
Two Unusual Cases of War Wounds of Heart. P. C. Samson.—p. 373.
Effect of Atropine on Gastric Secretion Following Thermal Trauma. H. Necheles, E. Prescott and W. H. Olson.—p. 382.
Bilateral Popliteal Hernia: Case Report. A. E. Sachs and L. Rubinstein.—p. 385.
Closure of Colostomy Stoma: Simplified Plan of Management. R. O. Gregg and J. M. Mosely.—p. 388.
Experiments in Ulcerative Enteritis: Failure to Produce it by Mesenteric Lymphatic Obstruction. E. S. Sinaiko and H. Necheles.—p. 395.
Split Thickness Skin Graft as Covering Following Removal of Fingernail. E. M. Hanrahan.—p. 398.

Heparin and Papaverine in Treatment of Gangrene.—McLean and Johnson report the history of a man aged 44 who developed gangrene in the foot following trauma, including tibial fracture and an accidental cut into the anterior lower part of the leg. As a result of inadequate supply of blood to the foot, signs of beginning gangrene appeared. It was decided to try to improve the circulation by the use of heparin, papaverine hydrochloride and the principle of intermittent venous occlusion. Heparin was used to increase the fluidity of the blood. The papaverine was used for its effect in relaxing striated muscle of vessels. The apparatus for producing intermittent venous occlusion was operated for forty-five minutes every four hours for sixteen days. The triple treatment was begun five days and seven hours after the injury. At this time it appeared that amputation might be necessary eventually. The final tissue loss was small portions of the ends of the toes and all of the nails. Amputation was avoided and a satisfactory functioning foot obtained. Recovery usually is not expected after forty-eight hours' lack of blood.

Chemical Production of Prolonged Sympathetic Paralysis in Causalgia.—Rasmussen and Alessi say that the availability of a slowly absorbed local anesthetic agent (rectocaine) suggested the possibility of increasing the effectiveness of paravertebral injections in the treatment of causalgia by prolonging the resultant sympathetic paralysis. Rectocaine contains 5 per cent benzyl alcohol, propylaminobenzoate and procaine. The first patient had causalgia of the left arm. A paravertebral injection was done. Fifteen cc. of 2 per cent procaine was injected along the left side of the bodies of the first and second thoracic vertebrae, producing vasodilatation of the hand and typical Horner's syndrome within five minutes. The pain was relieved for one hour and then returned. Four days later the paravertebral injection was repeated. Before the needles were withdrawn, 2.5 cc. of rectocaine was injected into each. The sympathetic paralysis and relief of pain persisted for forty-eight hours, with the latter then returning. Since it was felt that the amount of rectocaine was insufficient, a third injection was done. After 5 cc. of procaine injected at each segment had again produced prompt sympathetic paralysis and relief of pain, 4 cc. of rectocaine was introduced into each of the two needles. This time the pain did not return, and the relief persisted throughout the follow-up period of ten weeks. A second patient with causalgia was treated in a similar manner and relief was obtained.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:319-352 (Sept. 7) 1946

Migraine and Sympathetic Nervous Pathways. G. F. Rowbotham. —p. 319.
Crash Helmets. H. Cairns.—p. 322.
Penicillin in Treatment of Common External Eye Infections. J. Minton.—p. 324.
Hypersomnia Associated with Abnormal Hunger: Kleine-Levin Syndrome. J. Ronald.—p. 326.
Xenopus Pregnancy Test. R. F. Milton.—p. 328.
Giant Urethral Calculus in Female. N. C. Lake.—p. 328.

2:353-408 (Sept. 14) 1946

Postgraduate Education and National Health Service. F. Fraser.—p. 353.
Some Principles in Selection of Medical Students. D. H. Smyth. —p. 357.
Analysis of Results of Test Given at University College, London, for Selection of Women Medical Students for Session 1945-1946. J. S. Wilkie.—p. 367.
Medical Council of India. A. H. Butt.—p. 369.
Examinations: Meditations on Painful Theme. Ff. Roberts.—p. 380.

2:409-448 (Sept. 21) 1946

*Incidence, Incubation Period and Symptomatology of Homologous Serum Jaundice. Nancy Spurling, J. Shone and Janet Vaughan.—p. 409.
Postoperative Activity and Resumption of Normal Movement: Their Influence on Embolism and Thrombosis. G. Fitzgibbon.—p. 413.
Inability to Work in Tropical Climate. H. J. Trenchard.—p. 416.
Feces in Sprue. D. A. K. Black, P. Fourman and P. Trinder.—p. 418.
World Health Organization. M. D. Mackenzie.—p. 428.

Homologous Serum Jaundice.—Spurling and her associates made a follow-up study of 2,040 patients transfused with pooled serum and/or plasma, of 1,284 patients transfused with whole blood only and of 1,284 control patients not transfused. The incidence of jaundice in the patients receiving pooled plasma or serum was 7.3 per cent. Frank homologous serum jaundice did not develop in any patient receiving whole blood. Jaundice did not develop among the controls within five months of transfusion. The character of the jaundice was with one exception mild. The symptomatology and incubation period were in accord with previous accounts. To minimize the risk of homologous serum jaundice after transfusion, (1) human serum for prophylactic purposes should not be pooled, (2) for transfusion purposes only small pools should be used, (3) all blood products issued should carry an identification number, (4) records should be kept of the number of the bottle given to a particular patient and (5) machinery should be maintained for the notification of jaundice following transfusion, thus enabling the withdrawal of icterogenic material from circulation.

Edinburgh Medical Journal

53:401-464 (Aug.) 1946

Sensitivity of Bacteria to Action of Penicillin. J. P. Duguid.—p. 401.
Wartime Advances in Medicine Which Might Be Translated Into Civil Practice. A. Biggam.—p. 413.
Problem of Bacterial Variability and Origin of Infectious Disease. W. M. Levinthal.—p. 429.
Rheumatic Encephalopathy. D. Leys.—p. 444.
Case of Blackwater Fever Observed in Britain. H. Dlugosz.—p. 450.

Indian Medical Gazette, Calcutta

81:225-280 (June-July) 1946. **Partial Index**

Surgery of Divided Digital Tendons. F. V. Stonham.—p. 225.
*Some Not Well Known Manifestations of Riboflavin Deficiency. C. Gopalan.—p. 227.
Analytical Study of Intestinal Protozoal Infection, with Special Reference to Amebiasis. R. N. Chaudhuri and M. N. Rai Chaudhuri.—p. 230.
Effect of Sulfadiazine and Penicillin on Experimental Animal Plague. J. C. Gupta, G. Panja and M. Chatterjee.—p. 234.
*One Thousand Cases of Bubonic Plague Treated in an Emergency Plague Hospital. A. T. W. Simeons and K. D. Chhatre.—p. 235.
Electron Microscope and Its Use in Biology. A. N. Sen.—p. 247.

Riboflavin Deficiency.—Gopalan found that genital symptoms of riboflavin deficiency occur chiefly during the childbearing age. Of 67 females who presented genital symptoms in association with other signs of riboflavin deficiency and in whom these symptoms cleared on the administration of riboflavin, 64 were adult women and 3 were children. The minimal genital manifestation of riboflavin deficiency in women is an increase in the normal vaginal secretion. The resulting leukorrhea is apparently the result of increased transudation through the vaginal walls. Pruritus vulvae is present in cases of profuse leukorrhea. The leukorrhea abates on treatment with riboflavin, and the pruritus and vulvitis also subside. Pruritus ani, perianal inflammation and anal fissure are among the signs of riboflavin deficiency. Treatment with 10 mg. of riboflavin daily by mouth for two to four weeks leads to rapid healing of the fissure and subsidence of other signs. Scaly dermatitis of the scrotum is frequent in subjects with riboflavin deficiency, but preputial ulceration is also observed. Both these conditions are seen much more often in men than in boys. Among 92 cases of riboflavin deficiency in men above 18 years, 59 showed scrotal dermatitis which was associated with ulceration of the preputial margin in 32 cases; 3 cases showed preputial ulceration without scrotal involvement. In several cases of riboflavin deficiency observed by the author, the angles of the lids showed ulceration. He designates this condition as angular blepharitis.

Bubonic Plague.—Simeons and Chhatre say that 1,039 persons with plague were admitted to an Emergency Plague Hospital from the end of July 1945 to the middle of January 1946. There were 19 with nonbubonic plague, all of whom died. Of the remaining 1,020 patients 20 were treated by various methods and with apparently insufficient sulfonamide doses before a fixed routine was established. There remained 1,000 consecutive patients with bubonic plague who received a carefully supervised treatment with sulfathiazole or sulfadiazine. Sulfathiazole was injected intramuscularly and sulfadiazine intravenously. When sulfathiazole was injected, sulfathiazole tablets were given by mouth; when sulfadiazine was injected, only sulfadiazine tablets were given in addition. Two injections (1 Gm. each in adults) were given daily and two tablets four hourly day and night. This was continued until the temperature stayed below 100 F. for at least eight hours; from then on only tablets were continued. Some patients had as many as nineteen injections. Liberal use was made of dextrose-saline infusions, nikethamide, digilanid, vitamin C, bromide and morphine. Attention was paid to an adequate fluid intake. Early treatment seems to be important. The mortality rate among patients treated within the first twenty-four hours is 6.61 per cent, whereas after twenty-four hours it rises to 19.67 per cent. In 1,000 patients the mortality was 18 per cent; excluding moribund patients the mortality was 8.48 per cent.

J. of Neurol., Neurosurg. and Psychiatry, London

9:41-80 (April) 1946. **Partial Index**

Familial Disease Characterized by Noncalcifying Corticomeningeal Diffuse Angiomatosis and Progressive Demyelinization of White Substance. P. Divry and L. van Bogaert.—p. 41.
Subarachnoid Dissemination of Spinal Tumors. J. E. A. O'Connell. —p. 55.
*Etiology and Pathogenesis of Acute Sporadic Disseminated Encephalomyelitis and Multiple Sclerosis. M. S. Margulis, V. D. Soloviev and A. K. Shubladze.—p. 63.

Disseminated Encephalomyelitis and Multiple Sclerosis.—Margulis and his co-workers isolated two strains of filtrable virus—from the blood of 1 patient and from the cerebral tissue of another with acute disseminated encephalomyelitis. These strains have proved to be identical and to differ from other known human neurotropic viruses. The syndrome of acute disseminated encephalomyelitis has been produced in animals by means of inoculation with this virus. The morphologic picture obtained has proved identical, particularly in rabbits and puppies, to that found in man with acute disseminated encephalomyelitis. An attempt has been made to neutralize the virus thus isolated with the serums of patients suffering from acute disseminated encephalomyelitis and multiple sclerosis. The virus has been neutralized by serums from 50 per cent of patients with multiple sclerosis and from 70 per cent of patients with disseminated encephalomyelitis. These positive neutralization tests suggest that acute disseminated encephalomyelitis and multiple sclerosis have the same cause in some patients, while in others the same anatomic and clinical syndromes may be elicited by other agents or possibly by the same agent but with a different antigenic structure. Specific vaccine therapy has yielded satisfactory results in a small number of patients with acute disseminated encephalomyelitis and multiple sclerosis. There has been clinical improvement with considerable increase of antibodies in the blood.

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Lancet, London

2:293-332 (Aug. 31) 1946

Myth and Mumpsimus. J. R. Forbes.—p. 293.
Medical Photography: Review. P. Hansell.—p. 296.
Hospital Photographic Department. B. Stanford.—p. 299.
Anatomic Models in Teaching. R. de Seigneux.—p. 302.
Children Who Spend Too Long in Bed. J. A. McCluskie.—p. 302.

2:333-368 (Sept. 7) 1946

Epidemic Thrombophlebitis in East Africa Command. P. E. C. Manson-Bahr and A. D. Charters.—p. 333.
Nausea and Vomiting of Pregnancy: Study in Psychosomatic and Social Medicine. G. G. Robertson.—p. 336.
Calf Plasma or Serum for Transfusion. J. M. Massons.—p. 341.
*Typhoid Carriers Treated with Penicillin and Sulfathiazole. C. H. Comerford, H. Richmond and W. W. Kay.—p. 343.
*Pyridoxine (Vitamin B6) in Epilepsy: Clinical Trial. J. T. Fox and Gladys M. Tullidge.—p. 345.
Primary Diphtheria of Conjunctiva: Report of 2 Cases. A. R. Miller and D. E. Blower.—p. 345.
Peritoneal Nodules of Unknown Etiology. H. Ibrahim.—p. 346.

Penicillin and Sulfathiazole for Typhoid Carriers.—Comerford and his associates employed both sulfathiazole and penicillin on 2 established carriers, both of whom regularly excreted Bacterium typhosum phage type D, in their feces, 1 of them even after cholecystectomy. An initial dose of 2 Gm. of sulfathiazole by mouth was followed by 1 Gm. at four hour intervals. Approximately 500,000 units of penicillin dissolved in 10 cc. of sterile water was given intramuscularly at the same time. The treatment was continued for eight and seven days respectively, the total doses of penicillin amounting to over 24 million and 21 million units. Bacteriologic examination of every stool after treatment failed to reveal the presence of Bact. typhosum in them for periods of over one hundred and thirty days in the 1 case and over one hundred and sixteen in the other. Two months after treatment both patients showed reduced agglutination titers to typhoid-Vi antigen.

Pyridoxine in Epilepsy.—Since it had been observed that pigs and rats deprived of pyridoxine developed typical epileptic fits, Fox and Tullidge decided to try medication with pyridoxine on 8 epileptic school boys, who were selected because of the regularity of their fits. Doses of 20 mg. or 100 mg. each day were tried for weeks, but there was no evidence of a decrease in fits in any of the patients. The authors conclude that it is unlikely that pyridoxine would be of value in epilepsy.

2:369-404 (Sept. 14) 1946

*Painful Feet in Prisoners of War in Far East: Review of 500 Cases. E. K. Cruickshank.—p. 369.
*Folic Acid in Treatment of Megaloblastic Anemia. L. S. P. Davidson and R. H. Girdwood.—p. 373.
Confusion of Ameboma with Carcinoma. M. J. Smyth.—p. 376.
Gout in Leukemia: Report of Case. L. M. Shorvon.—p. 378.
Tuberculous Abscess Following Intramuscular Penicillin: Report of Case. D. Ebrill and S. D. Elek.—p. 379.
Light Weight Oxygen Mask of Plastic Material. B. S. Kent.—p. 380.
Picrotoxin in Barbiturate Overdosage. T. N. Misir.—p. 381.

Painful Feet in Prisoners of War in the Far East.—According to Cruickshank the symptom known as painful feet, burning feet or happy feet appeared among prisoners of war in Changi Camp, Singapore, at the end of July 1942, five and a half months after capture. This report is based on 500 personally observed cases. A dull ache was usually the earliest abnormality and was felt below the heads of the metatarsals and in the balls of the toes. At first it was present only at night after a long day's standing or walking. Later the ache became more pronounced, coming on in the early morning and increasing when the patient retired to bed. Sharp stabbing pains became superimposed on the ache in 58.6 per cent of the 500 cases. A single pain lasted from half a second to two seconds, shooting, parallel to the toes and soles of the feet, into the heels, through the ankle joints and sometimes up the shins to the knees. In 6.4 per cent there were similar symptoms in the hands, but these usually developed only in long-standing cases four to eight weeks after the onset of symptoms in the feet. The symptom developed when the diet of the prisoners was deficient in protein and the vitamin B complex. Hypertension and exaggerated tendon reflexes were added features in some cases. The diet records and the beneficial effect of treatment with nikethamide (the diethylamide of nicotinic acid) point to a deficiency of nicotinic acid, perhaps in conjunction with riboflavin deficiency, as a major factor in the production of the syndrome.

Folic Acid in Treatment of Megaloblastic Anemia.—Davidson and Girdwood employed folic acid in the treatment of 9 patients with megaloblastic anemia. Of the 6 patients with addisonian pernicious anemia 4 were treated with folic acid daily by mouth in doses ranging from 5 to 20 mg.; 2 received a single large dose by the parenteral and oral route respectively. Of the patients receiving daily oral treatment, only the 1 who received 20 mg. daily had a reticulocyte response and red cell rise completely up to the standard demanded by the U. S. P. board. Two others, who received 10 mg. daily by mouth, showed suboptimal rises in reticulocytes. The patient who received 5 mg. daily had a rise in erythrocytes that conformed to the U. S. P. standard, but the reticulocyte rise was suboptimal. In all 6 cases the bone marrow was transformed from a megaloblastic to a normoblastic state. The clinical state of the patients improved coincidentally with the blood. A patient who was given 200 mg. of folic acid intramuscularly in the first day of treatment showed a sharp rise of reticulocytes and an increase of more than 1 million red cells and 20 per cent hemoglobin in eleven days. In the sixth patient an excellent response resulted from a single dose of 400 mg. orally. If such a response can be obtained regularly, the simplest and most effective method of treatment may prove to be an initial large dose followed at weekly or fortnightly intervals by doses of 50 to 100 mg. Three patients with megaloblastic anemia which had been refractory to "anahaemin" responded to folic acid, which was, however, unable to restore the blood to normal. Since 2 of these patients had previously responded to proteolyzed liver, it is suggested that folic acid might be the active principle of proteolized liver.

Medical Journal of Australia, Sydney

2:181-216 (Aug. 10) 1946

Seasonal Variations in Ascorbic Acid Content of Australian Diet. M. Honey.—p. 183.
Basis of Postoperative Treatment in Appendicitis and Peritonitis: Folklore or Physiology? V. J. Kinsella.—p. 190.
*Use of Gamma Globulin in Prophylaxis of Measles. S. G. Anderson and W. M. Ket.—p. 196.
Insertion of Transfusion Needle Made Easy. T. A. Merton.—p. 197.

Gamma Globulin in Prophylaxis of Measles.—Anderson and Ket report that during an epidemic of measles in Melbourne 116 children who were closely exposed to infection were given gamma globulin prophylactically. About half of the children received 0.1 cc. of gamma globulin per pound of body weight; most of the others received 0.025 cc. per pound of weight. Sixty-seven of the children did not develop measles, 46 had a modified attack and in 3 the course of the disease was apparently uninfluenced by globulin. Of those who had received the larger dose, more than three fourths remained free from measles, whereas of those receiving the smaller dose more than half developed a modified attack but there were no complications. The 3 patients in whom the course of the disease was apparently uninfluenced had received the smallest prophylactic dose.

Transactions Royal Soc. Trop. Med. & Hyg., London

40:1-102 (Aug.) 1946

Distribution of Immunity to Yellow Fever in Central and East Africa. A. F. Mahaffy, K. C. Smithburn and T. P. Hughes.—p. 57.
Incidence of Sicklemia in West Africa. G. M. Findlay, W. M. Robertson and F. J. Zacharias.—p. 83.
*Cooley's Anemia: Notes on 6 Adult Cases. A. L. Fawdry.—p. 87.
Penicillin in Treatment of Experimental Relapsing Fever in Rats. E. S. Anderson.—p. 93.
Collapse of Lung and Porocephalosis. F. E. Stock.—p. 101.

Cooley's Anemia.—Fawdry says that the laboratory test which most strikingly shows the presence of Cooley's anemia is the plotting of the fragility curve. The harboring of the trait is of no consequence to the individual, though it may be to his offspring, so he usually survives unrecognized to adult age. The author reports 6 cases that represent the intermediate group which reaches and passes puberty but yet may be seriously incapacitated. All 6 patients showed splenomegaly, hypochromic erythrocytes and increased resistance of the cells to hemolysis by hypotonic saline solution. One patient showed a great increase of normoblasts in the marrow. Two were typical

of the mildest degree of the affliction: the first had no symptoms directly referable to his blood dyscrasia and the second only the icterus of the conjunctivas and a large spleen. As they do not have anemia, there has been no interference with their physical capabilities. Except possibly for lifelong repeated transfusions, which is scarcely practicable in Cyprus, there is as yet no therapy whereby the anemic patient can be restored to health and usefulness in the community. The milder form of the disorder is fairly frequent throughout the island.

Lyon Chirurgical, Paris

41:129-256 (March-April) 1946

Regeneration and Reconstitution of Dissected Nerves. A. Weber. —p. 129.
Postoperative Aspect of Peptic Ulcer: Sixty-Two Personal Observations. P. Santy, R. Chattot and J. Clert.—p. 138.
Extensive Embolism of Pulmonary Artery. R. Leriche.—p. 143.
*Prevention of Hemorrhagic Complications in Biliary Tract Surgery with Vitamin K. P. Mallet-Guy, R. Jeanjean and J. Ronchet.—p. 160.
*Two Recent Observations of Gangrene of Extremities of Venous Origin. R. Fontaine and E. Forster.—p. 173.
Adenocarcinomas of Cervix Uteri: Discussion of Choice of Therapeutic Indications. M. Dargent and R. Bonniot.—p. 180.
Exeresis in Treatment of Inveterate Suppuration of Parenchyma of Lungs. V. Aubert.—p. 188.
Toxic Diffuse Goiter and Myopathy. R. Peycelon.—p. 196.

Vitamin K and Biliary Tract Surgery.—Mallet-Guy and his associates employed prophylactic vitamin K treatment in 225 cases of biliary tract surgery. Only 63 patients had a normal prothrombin level, while 162 patients had a prothrombin deficiency. Preoperative determination of the prothrombin level is advisable in all cases of chronic icterus and in cases with a history of jaundice or of previous involvement of the common bile duct in the absence of chronic icterus. There was not a single death from a postoperative hemorrhage in a three year period during which biliary tract patients with hemorrhagic diathesis were treated with oral administration of 200,000 international units for twenty-four hours combined with a subcutaneous injection of 10 mg. of vitamin K when the prothrombin deficiency amounted to 20 per cent of the normal level or where the urgency of the surgical intervention required a rapid improvement of the prothrombin level. This treatment should be continued for two to three days prior to intervention. In cases in which the prothrombin level oscillates around 75 per cent of the normal, 150,000 units should be given by mouth for four to six days. In cases of icterus this treatment should be combined with oral administration of 1 Gm. of biliary extract for every 150,000 vitamin K units. Continuation of the satisfactory effect is ensured by a maintenance treatment with a twenty-four hour dose of 100,000 to 150,000 units for several days after the intervention.

Gangrene of Venous Origin.—Fontaine and Forster report 2 cases of venous gangrene. A man aged 40 presented a thrombophlebitis of both lower extremities after a hemorrhoidectomy. After several weeks extensive skin gangrene involving the anterior aspect of the right leg and foot had separated, and grafting of the granulating surface of the wound became possible. Mummification of four toes of the left foot occurred. Residual edema and loss of the toes was a much better result than could have been expected. It shows that venous gangrene, although associated with a massive slough, may be limited to the skin. A boy aged 8 years fell on his arm, an erroneous diagnosis of fracture of the elbow was made and a plaster cast was applied. Moist gangrene of the hand and the inferior third of the left forearm occurred within a few days. X-ray examination revealed the absence of any fracture. Amputation became imperative because of the severe massive gangrene. Microscopic examination of the amputated extremity showed thrombosis of all the veins, while the arteries were normal. Rich collateral venous circulation is responsible for the fact that venous gangrene occurs only after extensive obliteration of the veins. Poor general condition or associated arterial spasm can favor the occurrence of venous gangrene but is not indispensable to it. Anoxemia resulting from venous stasis due to deficient collateral circulation is responsible for the occurrence of venous gangrene.

Progrès Médical, Paris

74:305-336 (July 24) 1946

Penicillin and Anaerobic Microbes. A. Lemierre.—p. 307.
Microbic Antagonism in General and with Particular Reference to Antibiotic and Antidote Properties of Culture Filtrates of B. Subtilis and of Penicillium Notatum Concerning Certain Pathogenic Bacteria and Microbic Toxins: Practical and Theoretical Consequences. G. Ramon and R. Richou.—p. 309.
*Therapeutic Value of Procaine Hydrochloride Infiltration of Lumbar Sympathetic Ganglions in Arteritis. P. Wertheimer, P. Frieh and R. Gautier.—p. 319.

Procaine Infiltration of Lumbar Sympathetic Ganglions in Arteritis.—Wertheimer and his associates infiltrated the lumbar sympathetic ganglions with procaine hydrochloride as the only method of treatment in 38 cases of arteritis with calcareous infiltration in persons whose average age was 65 years. Ischemic gangrene supervened in 12 of the cases. Good results were obtained in 22 cases, stabilization took place in 4 cases, amputation was performed in 8 cases and death occurred in 4 cases. Good results were obtained in 7 of the cases with gangrene, rapid death occurred in 2 and amputation became imperative in 3, with death in 1 of them. The periods of observation varied from six to nine years in 10 cases, from three to four years in 4 cases and from one to two years in 11 cases. Amputation need not be considered as absolute failure of treatment, since in 3 cases a temporary improvement lasting for six months to three years was obtained prior to amputation. In the majority of the cases repeated infiltrations of lumbar sympathetic ganglions were required. The good results, particularly those in cases of gangrene, suggest that in the long run repeated procaine hydrochloride infiltrations of lumbar sympathetic ganglions may have the same effect as sympathectomy, but this hypothesis requires further control.

Gynaecologia, Basel

121:225-340 (May-June) 1946

Effect of Demerol on Delivery. F. de Senarclens.—p. 225.
Effect of Spasmolytics on Period of Dilatation During Birth (Investigation of the New Spasmolytic "Hexacompal"). H. Sauter.—p. 247.
*Necrosis of Renal Cortex and of Anterior Lobe of Hypophysis During Pregnancy: Contribution to Morphology of Eclampsia. W. Hügin. —p. 269.
*Presence in Human Sperm of a Ferment (Hyaluronidase) Which Splits Mucin: Contribution to Problem of Disturbances in Male Fertility. E. Eichenberger.—p. 288.
Dermoid Cyst with Cancerous Degeneration of Thyroid Tissue. J. H. Müller.—p. 330.

Necrosis of Renal Cortex and of Anterior Pituitary During Pregnancy.—Hügin reviews the histories of 2 pregnant women who developed severe eclampsia with anuria and intrauterine death of the fetus. Both women died and necropsy revealed the hitherto unknown combination of necrosis of the renal cortex and of the anterior lobe of the hypophysis. The microscopic changes are described and evaluated. These changes and reports in the literature indicate that the disorder in question represents a toxic disturbance of pregnancy in which there may occur severe changes in the tubular and vascular portions of the kidney, with total infarction of the renal cortex and necrosis of the anterior pituitary, and both organs usually show extensive vascular thrombosis. The tissue changes are mainly degenerative in nature; inflammatory changes occur less frequently.

Mucin Splitting Ferment in Human Sperm.—Eichenberger studied 76 sperm specimens from 53 men, the majority of whom had proved sterile over more than two years of marriage and requested examination on this account. The author found in normal human semen a ferment having qualities identical with those of hyaluronidase. There is usually a parallelism between the number of spermatozoa and the hyaluronidase contents of the sperm. Semen which does not contain spermatozoa shows no hyaluronidase activity. Spermatogenesis and production of hyaluronidase must be considered as two processes which condition each other reciprocally and are inseparable. The fermentative insemination theory explains the rapid decrease of fertility in males whose semen contains less than 60 million spermatozoa per cubic centimeter of semen.

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Schweizerische Zeitschrift für Tuberkulose, Basel

3:69-164 (No. 2) 1946

Aschoff-Klinge Node in Myocardium of Patients with Tuberculosis of Lungs. H. de Courten.—p. 69.
*New Investigations on Besnier-Boeck-Schaumann Disease (Epitheloid Cellular Granulomatosis). S. J. Leitner.—p. 108.
Clinical Features of Tuberculosis in Children. J. Rutishauser-Scharpf. —p. 134.
Pseudolithiasic Type of Tuberculosis of Kidneys (Tuffier). R. Allemann. —p. 149.

Besnier-Boeck-Schaumann Disease.—Leitner reports 8 cases of Boeck's disease in 5 male patients between the ages of 9 and 54 years and in 3 women between the ages of 25 and 43 years. The tuberculous etiology of Boeck's disease is strongly suggested by the transition from benign granulomatosis to tuberculosis in 3 of these cases, by the simultaneous occurrence of osteitis tuberculosa multiplex cystoides and of tuberculosis in the bones in 1 case, and by the tuberculin test changing from negative to positive in 4 cases. The similarity of the clinical symptoms and of the course of benign granulomatosis in a brother and sister suggests that the constitution plays an important part in the course of Boeck's disease. The tuberculin test was slightly positive in the sister and negative in the brother. In 1 case benign granulomatosis occurred after a primary infection. The microscopic picture of this case with its small caseous masses suggests that the transition from the allergic condition of the primary infection to that of the benign granulomatosis was not yet terminated and that the caseous masses depended on the allergy which preceded Boeck's disease. The concept of Boeck's disease as a specific type of tuberculosis explains the fatal course in 2 of the author's cases. The tuberculin reaction is to be considered as an antigen-antibody reaction. The negative tuberculin test in benign granulomatosis may be the result of the fixation of the antibodies at the site of their production (the reticuloendothelial system) by the antigens of the Koch bacillus which are destroyed at the same site. The reticuloendothelial system is to be considered as the central factor in the defense mechanism; an immunity such as can be produced in animals or human subjects by desensitization, but not an anergy, may be observed in benign granulomatosis with its productive reticuloendothelial system reaction. A real anergy may be observed in acute tuberculous septicemia characterized by nonspecific necrosis, abundant bacilli and a very rapid malignant course. The absence of tissue defense in the reticuloendothelial system may be responsible for the negative tuberculin test. Benign granulomatosis differs from generalized caseous tuberculosis of the lymphatic system, which in spite of the same localization is characterized by a generalized and uniform caseous process and by its malignant course.

Revista Médica de Chile, Santiago

72:377-444 (June) 1946

Sulfanilamide Therapy in Hepatobiliary Infections. R. Armas Cruz, G. Lira and A. Spencer.—p. 377.
Cancer of Gallbladder. R. Vargas Molinare and A. Larach N.—p. 384.
Myelosclerosis: Present Aspects of Diagnosis; Treatment. A. Nijamkin, R. Etcheverry, P. García Palazuelos, P. Fernández and R. Barahona. —p. 387.
*Methyl Testosterone and Addison's Disease. A. Atria R., L. Vargas F. and Renato Sanz del Fierro.—p. 394.
Treatment of Nontuberculous Acute Pleural Empyema with Intrapleural Penicillin. G. Sepúlveda D.—p. 397.
Horseshoe Kidney. R. Vargas Zalazar.—p. 402.

Methyl Testosterone and Addison's Disease.—In studying the action of testosterone on uterine fibromyoma, Atria and his co-workers found that the subcutaneous implantation of tablets of methyl testosterone exerted a noticeable influence on the pulse and the arterial pressure, whereas testosterone propionate did not have the same effect. Because of this observation the authors decided to try implantation of methyl testosterone in cases of adrenal insufficiency. In a man aged 37 and a woman aged 40 subcutaneous implantation of methyl testosterone corrected the subjective disturbances and the main clinical signs of chronic adrenal insufficiency. In the first patient 120 mg. of methyl testosterone was implanted into the gluteal region and in the second patient 100 mg. Seventy days after the implantation the first patient was still in a favorable condition. The authors stress the prolonged effect in relation to the low dose. The low dosage has the advantage that it eliminates the excessive dosage of desoxycorticosterone and the masculinization in female patients.

Wiener medizinische Wochenschrift, Vienna

96:281-304 (Aug. 1) 1946

Static Disorders of Lower Extremity. A. Saxl.—p. 281.
*Investigation on Gonadotropic Neurosecretion. K. Richter and Sybille Schiler.—p. 284.
*Administration of Eupaverin in Surgical Intervention for Arterial Embolism. O. Bruckschwaiger.—p. 286.
Disturbance of Permeability of Erythrocytes to Rhodan Salts in Soldier with War Nephritis. E. Fieber, W. Pilgerstorfer and D. Roller. —p. 288.
Case of Mastoiditis Causing Recurrent Pneumonia and Dyspepsia with Atrophy in Infant. P. Krepler.—p. 291.

Gonadotropic Neurosecretion.—Increasing amounts of anterior lobe of the pituitary, of diencephalon and of uncus substance of dogs were implanted into infantile albino rats by Richter and Schiler. Occasionally guinea pigs and rats were used as donors. In addition to the microscopic criteria of the gonadotropic effect of these substances on the infantile rat ovary the weight of the ovaries and uteri of the animals experimented on was ascertained, adding an objective measure of the intensity of the gonadotropic reaction elicited by the implantation. The increase in weight of the ovaries and of the uteri paralleled the weight of the implanted amount of the anterior pituitary lobe substance. The weight of the ovaries and of the uteri of the rats varied between the upper and lower normal limit when increased amounts of diencephalon and uncus substance were implanted. A gonadotropic reaction thus resulted only from the anterior pituitary lobe implants and not from those of the diencephalon or uncus substances. The tuber cinereum, therefore, cannot be considered as the site of production of gonadotropic hormones. Destruction of the gonads and disturbances of the sexual impulses resulting from electrocoagulation of the tuber cinereum suggest that the tractus supraopticohypophyseos but not a "nervous center" has been destroyed. The tractus supraopticohypophyseos is to be considered the route by which the nervous impulses which are continuously needed for its support and regulation are conveyed to the pituitary. It may be that the chemical process occurring in the terminal branches of the tractus supraopticohypophyseos is similar to that which occurs in the transmission of stimuli to vegetative and motor nerves.

Eupaverin in Arterial Embolism.—A case of bilateral embolism of the axillary artery in an adipose woman aged 77 is reported by Bruckschwaiger. The emboli were removed under local anesthesia and the arteries were sutured. Immediately afterward a narrowing of the vessels was observed at the suture site and peripherally; the vessels were pulseless. An injection of 0.06 Gm. of methylene-dioxy-benzyl-methylmethylene-dioxyisoquinoline (eupaverin) in 2 cc. was made into the artery above the suture site. The width of the artery was restored to normal within a few seconds and the pulse in the radial artery became definitely palpable. The patient complained about unpleasant formication and "awakening" of the hand. The livid color of the skin turned to a healthy red. The extremity became warm and sensory perception was restored. Normal function of both upper extremities resulted four weeks after the surgical intervention. Early surgical treatment of arterial embolism combined with administration of eupaverin may prevent failure of embolectomy, while conservative treatment of embolism of the iliac, femoral and axillary arteries with eupaverin may be harmful. The spasmolytic effect of the drug may cause the embolus to migrate to another site where its surgical removal would be more difficult. Consultation of the internist with the surgeon prior to the administration of eupaverin is imperative in all cases of arterial embolism and particularly in circulatory disturbances of the extremities associated with typhus.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

90:719-758 (June 29) 1946

*Endocrine Disturbance with Manifestations of Nontropical Sprue and of Addison's Disease. A. L. de Groot.—p. 720.
Significance of Smooth Muscle Tissue in Aorta in Connection with Ruptures in Media. A. A. van der Kroon.—p. 725.
*Treatment of Bronchial Asthma with Small Doses of Copper. F. W. Klaarenbeek.—p. 730.
Treatment of Camp Eyes (Deficiency Amblyopia). J. G. van Manen.—p. 733.
Amenorrhea in Women's Camp at Tangerang. C. M. Hart-Meerloo and A. Scheltema-Joustra.—p. 736.
Early Stage of Gastric Cancer. J. A. Arendsen Hein.—p. 739.
Treatment of Injuries in Region of Finger Nail. B. Veraart.—p. 743.

Nontropical Sprue Combined with Addison's Disease.—A man aged 52 complained of loss of weight, fatigue, painful tongue, dry mouth and thin foamy stools of light color. The sense of smell was reduced, and coughing brought up mucus. The hands and feet were cold, and the feet were swollen. Years before the patient had had joint disorders and had been treated with gold preparations. After that symptoms appeared which were similar to those he had now. In the differential diagnosis the disease of Besnier-Boeck and tuberculosis were considered but ruled out. Many symptoms indicated nontropical sprue, but there were also some, particularly the diffuse pigmentation of the skin and mucous membranes and hypotension, which suggested Addison's disease. A combination of these two diseases was accepted. While it has been established that Addison's disease is the result of a disorder of the adrenal cortex, it has been suggested by Verzár that this is true also of nontropical sprue. As a corroboration of this opinion de Groot found that many symptoms of sprue improved noticeably under treatment with a preparation of the adrenal cortex.

Copper in Treatment of Bronchial Asthma.—Klaarenbeek obtained favorable results with a copper preparation in patients with bronchial asthma. Best results were obtained in patients up to 20 years of age. He reports 7 additional cases of bronchial asthma in which the copper preparation was used. All of these patients were less than 26 years of age. The copper preparation had been used by others in polyarthritis and certain forms of tuberculosis. It produces favorable results in young asthma patients. The dosage must be adjusted for the individual patients. According to the usual scheme two injections of 10 and 25 mg. respectively are given during the first week. One injection of 50 mg. is given weekly during the following four weeks. If the attacks cease, 100 mg. can be given every other week, but if this is not the case 100 mg. or more should be given every week until the attacks stop. The effective dose can be given for four weeks, and after that the aim should be to prolong the interval by one week after four injections. One or two injections per month will usually suffice.

90:759-798 (July 6) 1946. **Partial Index**

*Behavior of Blood Pressure During Periods of Starvation and Recovery (September 1944 to September 1945). S. Lups and C. Francke.—p. 764.
Spinal Conditional Reflexes. J. Ten Cate.—p. 769.
*Experiences in Treatment of Acute Bacillary Dysentery. W. J. J. Molenkamp.—p. 771.
Treatment of Lupus of Palate. B. J. Rienks.—p. 775.

Blood Pressure During Starvation and Recovery.—During the period of starvation, when loss of weight was observed in the majority of persons, Lups and Francke studied the relationship between the state of nutrition and the behavior of the blood pressure. They found that in April 1945, during the period of severest hunger, the systolic as well as the diastolic blood pressures were definitely lowered. In September 1945, when 80 per cent of the people examined had increased in weight considerably, the blood pressure had increased in 77 per cent of those with hypotension, in 47 per cent of those with normal pressure and in 25 per cent of those with hypertension. The authors think that the low rations, particularly the shortage of proteins, were responsible for the lowering of the blood pressure readings.

Treatment of Acute Bacillary Dysentery.—The observations reported by Molenkamp were made in a Japanese internment camp. He describes the pathologic changes taking place in the intestine, differentiating 3 stages: (1) the catarrhal stage, (2) the stage of crust formation and (3) the stage of cicatrization. In the treatment, rest is of great importance for the intestine. Dietetic measures were employed and in addition the combined administration of sulfaguanidine (5 times 1.5 Gm.) and tincture of opium (5 times 15 drops) for five days. When the patient suffered from constipation the opium was omitted. When necessary this treatment was repeated after several days. The treatment proved effective in acute, mild and moderately severe cases.

Vrachebnoe Delo, Kharkov

No. 6, 290-379, 1946. **Partial Index**

Peculiarities of Phagocytosis in Various Infectious Diseases. V. K. Stephanskiy.—p. 290.
Possible Significance of Bacterial Allergen in Septic Scarlet. S. M. Minervin, S. M. Fridman and T. M. Rozengart.—p. 293.
Blood Bacteriology in Wound Sepsis. G. M. Frenkel.—p. 295.
*Insulin Therapy of Ulcerative Disease. M. A. Yasinovskiy.—p. 310.
*Question of Formation of Renal Stones After Injury to Long Bones. A. P. Tsulukidze.—p. 343.

Insulin Therapy of Ulcerative Disease.—In treating 98 patients with gastroduodenal ulcer, Yasinovskiy administered insulin to 98, insulin and atropine to 69 and atropine alone to 37. Patients in the insulin group received 10 units of insulin twice daily, before breakfast and before dinner. All the patients received the usual bland ulcer diet plus 50 Gm. of sugar daily. The diet was adequate in calories and vitamins. Significant improvement was noted in 85 of the insulin group of 98, in 9 very little change was noted and in 4 there was exacerbation of the symptoms. Improvement therefore took place in 86.7 per cent. Of the 37 patients treated with atropine 35 showed definite improvement. In the group receiving combined insulin-atropine treatment, considerable improvement was accomplished in practically all cases. The duration of improvement in the insulin group lasted from three to twelve months. As a rule recurrence was brought about by dietetic errors. The insulin treated group and the atropine treated group presented a striking difference in the acidity of the gastric contents. The atropine group contained 60 per cent of patients with hyperacidity at the beginning of the treatment. On the completion of the treatment the group did not contain any instance of hyperacidity. In the insulin treated group the number of cases with hyperacidity not only did not diminish but increased from 47 per cent to 50 per cent. The group of patients treated with insulin and atropine occupied a median position, with the number of cases with hyperacidity reduced from 64 per cent to 28 per cent. The results obtained with insulin therapy of ulcerative disease suggest that there is no definite parallelism between the clinical course of peptic ulcer and acidity of the gastric contents. The effect of insulin cannot be explained alone by its action as an alkalizing factor and by its action on the vegetative nervous system. The author believes that its effect is also due to its action on a functionally inadequate liver and pancreas. Insulin therapy of ulcer is particularly indicated in cases of hypochlorhydria in the presence of advanced emaciation associated with involvement of the pancreas and the liver.

Renal Stones After Long Bone Injury.—Tsulukidze states that, of 45 combat men admitted to his clinic because of renal stones, 8 gave a history of gunshot wounds. Four of these had gunshot wounds of the thigh and leg. Analysis of 184 postmortems of men with trauma of the bones of the lower extremity revealed the presence of renal stones in 5, 4 sustained a fracture of the thigh and 1 a gunshot fracture of both legs. Pathologists not infrequently record the presence of sand in the kidneys in subjects with bone injury, particularly of bones of the lower extremity. The role of bone injury in the formation of renal stones, according to a majority of authors, is due to an increase in the blood calcium and to infection. The author believes that fat embolism associated with fractures is another factor. Among other conditions favoring renal calculosis is the passive state of the patient and the diet. The passive state of the patient favors alteration in the blood circulation in the kidney and urinary stasis. Fat embolus lodged in the kidney can constitute an organic nucleus for deposition of salts. The fat embolism may also produce an infarct which will act as a nucleus for a stone. A septic embolus may be transferred to the kidney when a fracture of the bones of the lower extremity is complicated by thrombophlebitis.

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Book Notices

Surgical Treatment of the Nervous System. Supervising Editor: Frederic W. Bancroft, A.B., M.D., F.A.C.S., Associate Clinical Professor of Surgery, Columbia University, New York. Associate Editor: Cobb Pilcher, M.D., F.A.C.S., Associate Professor of Surgery, Vanderbilt University School of Medicine, Nashville, Tennessee. Cranial and Intracranial Surgery, Tumors, Epilepsy and Cranial Nerve Disorders, Spinal Cord, Autonomic Nervous System, Peripheral Nerves. Fabrikoid. Price, $18. Pp. 534, with 298 illustrations. Philadelphia, London & Montreal: J. B. Lippincott Company, 1946.

The editors of this excellent textbook have organized the efforts of neurosurgical authorities from various centers in the United States. The result is an exceedingly useful volume dealing with the many and highly diversified problems of surgery of the brain, the spinal cord and the peripheral and autonomic nervous systems. Each author presents all the known facts relating to the pathology, diagnosis and treatment of his subject. The chapters are interestingly written and easily assimilated, especially since there is little similarity between the literary styles of the various contributors. In the words of the editors, "a healthy diversification of opinion on neurosurgical problems as a whole" is obvious and is gratifying to the critical reader. The entire field of clinical neurologic surgery is covered in this fine work, including a chapter on chemotherapy. In the rapidly growing field of neurologic surgery there has been an urgent need for a thorough and authoritative textbook covering all the problems encountered in this specialty. Several previous textbooks have been excellent but are now outdistanced by the rapid developments in neurosurgery stimulated by the war. This single volume presents a comprehensive, authoritative and modern view of clinical neurosurgery. It should be a standard textbook for medical students and deserves to be read by every neurologic surgeon and by every other surgeon whose endeavors bring him into contact with the central, peripheral or autonomic nervous system.

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Environmental Warmth and Its Measurement: A Book of Reference Prepared for the Royal Naval Personnel Research Committee of the Medical Research Council. By T. Bedford. Medical Research Council, War Memorandum No. 17. Paper. Price, 9d., 25 cents; Including Supplement, 2s. 3d., 45 cents. Pp. 40, with 10 illustrations. London: His Majesty's Stationery Office, 1946.

This small and timely booklet sets forth in nontechnical language descriptions of the various instruments used in measuring environmental warmth—both radiant and kinetic—and the methods of evaluating the significance of their readings. The recent years of prolonged naval action in tropical waters brought a keen appreciation of the debilitating and efficiency lowering effects of hot environments on exposed personnel. Radiant and so-called wild heat became very important in combat vessels during periods of action or alert, presenting acute problems in personnel welfare and efficiency. Recognition of these problems and the need for their solution led to the preparation of this booklet as a first step in the collection of needed facts. The U. S. Navy already is air conditioning its newly constructed combat ships, and the beneficial results in improved health and efficiency of the ships' personnel are already obvious. Since workers in the medical sciences rarely have a clear appreciation of what radiant heat means in man's heat loss problem, this booklet is heartily to be recommended for their perusal. It is intended primarily as a working guide for those directly engaged in solving the Royal Navy's heat problems aboard ship.

Les tumeurs et les polypes du cœur: Etude anatomo-clinique. Par le Dr Ivan Mahaim. Préface du Professeur Dr. Jean-Louis Nicod. Monographie de l'Institut d'anatomie pathologique de l'Université de Lausanne. Paper. Pp. 568, with 67 illustrations. Paris: Masson & Cie; Lausanne: F. Roth & Cie, 1945.

The various tumors of the heart and their clinical manifestations are described. The book is divided into sections according to the location of the tumors. Thus, two hundred pages are devoted to "polyps" of the heart. Polyps are defined as tumors bulging into cardiac chambers, be they rhabdomyomas, lipomas, fibromas, myxomas or myxomatous thrombi. A serious criticism of the terminology of this book is that the differentiation between organized thrombi and myxomas is not clear: thus, a number of the tumors described are mural thrombi. Another unfortunate feature of the book is the lack of microscopic studies in some important cases.

Numerous observations illustrate the symptomatology and the various mechanical accidents caused by these "polyps." The accidents are classified into three types: (*a*) arterial embolism, (*b*) obliteration of a cardiac chamber, (*c*) occlusion of a cardiac orifice (tricuspid, mitral). Illustrating the first type, a case with embolism into the middle cerebral arteries is reported. The emboli were composed of "myxomatous appearing" connective tissue rich in blood vessels and histiocytes loaded with hemosiderin. The original "polyp" was found in the right auricle and was not examined microscopically but was classified, nevertheless, as a "myxomatous polyp." Emphasis is placed on the microscopic examination of the emboli because they represent biopsies of "cardiac polyps." Cardiac polyps are not inaccessible to surgery when they are benign. In some cases the "polyps" were primary spindle cell sarcomas or metastases from primary carcinomas of the kidneys or of the organs of reproduction.

In the second part of the book are described the benign "nonpolypoid" tumors of the heart. The hemangioblastoma and the benign mesothelioma belong to this group. The benign mesothelioma is a rare tumor, usually located in the septum near the Tawara node. It is believed to arise from epicardial inclusions in the septum. The symptomatology of this tumor is illustrated by carefully studied cases.

The malignant tumors of the myocardium are considered in the third part. They are classified as primary and secondary. Numerous histologic varieties of primary sarcoma of the myocardium are described. The relationship of the heart to the main bronchi and to the esophagus is reviewed. Metastases of primary extracardiac tumors reach the heart by direct extension or by the blood stream. An electrocardiographic examination should be made in every case of suspected cancer in order to detect myocardial involvement. The modification of the T wave does not have the characteristic evolution observed in myocardial lesions due to coronary sclerosis.

In the fourth part tumors of the pericardium are considered. Among the benign tumors, fibroma, lipoma, leiomyoma, lymphangioma and dermoid cysts are described. The malignant tumors of the pericardium (primary or metastatic) are associated with pericardial effusion (hemopericardium). Their symptomatology is reviewed and emphasis is placed on the x-ray picture and fluoroscopic examination.

The author believes that tumors of the heart are not rare and, if the internist looks for them as the neurologist looks for tumors of the brain, they will cease to be a pathologic curiosity.

Electrocardiography Including an Atlas of Electrocardiograms. By Louis N. Katz, A.B., M.A., M.D., Director of Cardiovascular Research, Michael Reese Hospital, Chicago. Second edition. Cloth. Price, $12. Pp. 883, with 525 illustrations. Philadelphia: Lea & Febiger, 1946.

The preface states that this edition has been expanded 50 per cent over the first, accomplished largely through the addition of more illustrations, summary tables, and a discussion of lead CF_5. But some of the length is attributable to a verbose and repetitious style which if corrected would not only shorten the book but make it more readable. The numerous illustrations, which are excellently reproduced, could be fewer in number, for many are examples of abnormalities adequately demonstrated in one or two illustrations rather than in six or seven, as is frequently done. The legends are too long and too detailed, and the main point to be emphasized is often thus obscured. References are numerous and up to date, but they are simply listed at the end of each section and not referred to in the text. There are an inordinately large number of typographical errors, considering that this is a second edition.

In the opening paragraph of section I there is a statement that "electrocardiographs are sensitive recording voltmeters." The string galvanometer is an ammeter. A little further on overshooting is ascribed to underdamping. Actually it is caused by the skin acting as a condenser with a by-pass resistance. These errors are typical of several others of an electrical and physiologic nature which occur in this section.

Section II, among other things, contains a description of electrocardiograms which bear such names as coronary pattern, heart strain pattern, digitalis pattern and rheumatic mitral pattern. There is also an axis shift pattern, the assumption

being that with a certain contour of the electrical record one may say that the apex of the heart has been rotated upward and to the left (left axis shift) or downward and to the right (right axis shift). For this particular pattern this is oversimplification, for the record obtained will depend not only on rotation of the heart about its anteroposterior axis but also on rotation about its longitudinal and transverse axes and on local alterations in conduction and depolarization as well as on other factors. But the nomenclature the author uses to describe all these patterns has considerable significance other than from the point of view of electrocardiographic theory. By giving anatomic names to physiologic phenomena he has made a great appeal to the physician who welcomes this tenuous short cut to the cause of electrocardiographic abnormalities. It makes clinical electrocardiography easy, and he can disregard such "difficult" concepts as the electrical axis and the ventricular gradient. Incidentally the author also disregards these in his book after giving an erroneous definition of the latter. In short, the book gives impetus to an inaccurate and most deceptive practice—the making of anatomic and physiodynamic diagnoses from a purely electrophysiologic method.

That this is unsound the author paradoxically admits in numerous places throughout the book. Further, he emphasizes many times the lack of correlation between the electrocardiographic and the anatomic. For example, on page 393 he lists no less than twenty clinical entities which give a "coronary-like contour."

An otherwise good section on arrhythmias (III) is marred by inclusion of their clinical management. Treatment does not belong in a book titled "Electrocardiography." Further, the subject matter, particularly on the treatment of auricular fibrillation, contains some statements recommending the use of quinidine when emboli are occurring, and favoring rapid digitalization in myocardial infarction, to which most experienced clinicians would probably take vehement exception.

The beginner will find the length and wordiness of the volume a real obstacle to complete assimilation; the electrocardiographer will find the illustrations useful for reference and teaching but the text confusing because it is often contrary to what he has read elsewhere; the expert will find much with which he will disagree.

Pneumoperitoneum Treatment. By Andrew Ladislaus Banyai, M.D., F.A.C.P., F.C.C.P., Associated Clinical Professor of Medicine, Marquette University Medical School, Milwaukee, Wisconsin. Cloth. Price, $6.50. Pp. 376, with 74 illustrations. St. Louis: C. V. Mosby Company, 1946.

This monograph is a complete presentation of the subject of pneumoperitoneum. The material has been prepared with great care and is clearly and concisely presented. In the chapter devoted to historical review it is pointed out that the idea of pneumoperitoneum was conceived in 1872, when a laparotomy for another purpose revealed the presence of tuberculous peritonitis from which the patient subsequently completely recovered. For some time thereafter laparotomy became the standard treatment for tuberculous peritonitis. Although the exact mechanism of the therapeutic action was not understood, several theories were advanced. The idea of introducing oxygen or air through a needle into the peritoneal cavity was later conceived and has since been used to a considerable extent. In the chapter on the technic of pneumoperitoneum every step is presented in detail. The complications of this procedure are presented, such as air embolisms, accidental pneumothorax, mediastinal emphysema and scrotal pneumocele. Several chapters are devoted to the therapeutic application of pneumoperitoneum in such conditions as tuberculous peritonitis, tuberculous enterocolitis, pulmonary tuberculosis, bronchial asthma, bronchiectasis, pulmonary emphysema and pulmonary hemorrhage of nontuberculous origin. The author has had a large experience with this form of treatment and he presents the advantages, disadvantages and ultimate results so free from bias as to give the reader extreme confidence in his work. Seventy-four well chosen illustrations and approximately five hundred references are included. This book contains a great deal of information concerning pneumoperitoneum which has never before been assembled in one volume. It can be highly recommended to all physicians.

Clinical Laboratory Diagnosis. By Samuel A. Levinson, M.S., M.D., Ph.D., Director of Laboratories, Research and Educational Hospitals, Chicago, and Robert P. MacFate, Ch.E., M.S., Ph.D., Assistant Director of Laboratories, Research and Educational Hospitals, Chicago. Third edition. Cloth. Price, $10. Pp. 971, with 207 illustrations. Philadelphia: Lea & Febiger, 1946.

This is a complete handbook, including chapters on skin tests, pediatric procedure, tropical medicine, legal medicine and toxicology, histologic technic and such recently developed procedures as penicillin assay and kidney clearance tests with inulin and diodrast. An appendix with important general data and laboratory procedures has been added. The indexing is excellent, and the additional index for important laboratory tests in the common diseases should be very useful. Preceding the descriptions of the technical procedures are introductory remarks about the normal functions and clinical pathology of each organ or system. In places these explanations are not up to modern concepts or are too vague to be adequate. The book has an abundance of illustrations, most of them clear and well chosen. A smaller number of the pictures are actual photographs, which show the important structures clearly. The drawings are good and the student will profit from them more than from photographed specimens. Concerning laboratory methods, the value of certain tests (e. g. stomach tests) seems to be overstressed and could be simplified. A number of the older tests could be omitted. Instead of some of the simple methods with doubtful accuracy, the newer more accurate methods (such as enzyme determinations) may be preferred, though they involve more work and experienced technicians. Obviously this book was not written for the man engaged in medical research but for the technician, the medical student and the medical practitioner.

A Textbook of Gynecology. By Arthur Hale Curtis, M.D., Professor and Chairman of the Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago. Fifth edition. Cloth. Price, $8. Pp. 755, with 455 illustrations, chiefly by Tom Jones. Philadelphia & London: W. B. Saunders Company 1946.

This edition of Curtis's book, for years one of the best of the standard textbooks, is larger than the others, retains the balance, the fine illustrations and the high literary standards of its predecessors and has, of course, been brought up to date. It would be superfluous to recount the contents of the volume, for it is complete. The character of the book does require comment. Curtis has a remarkable gift for making the reader feel that he is in private conference with the author. After presenting both sides of debatable issues fairly, Curtis tries frankly to win the reader over to his view. In these days when textbooks tend to be thoroughly documented, encyclopedic, impersonal and rather dry, it is refreshing to encounter an author who makes no attempt to camouflage his personal opinion. The fact that Curtis admits gracefully and with good humor that he may be in error in these personal views seems only to give them added weight. At the same time there is established between author and reader a feeling of friendly familiarity which is the pleasantest quality of the work. Authoritative but not dogmatic, sound, yet up to date, excellently illustrated, this textbook may profitably be read by any one interested in gynecology.

Urologic Roentgenology. By Miley B. Wesson, M.D. Second edition. Cloth. Price, $5.50. Pp. 259, with 258 illustrations. Philadelphia: Lea & Febiger, 1946.

This edition of a work recognized as authoritative has been so thoroughly revised and rewritten as to constitute a practically new book. The plates have been gone over carefully and many old ones discarded and new ones added. The book is an intensely personal one, and the strong convictions and opinions of Dr. Wesson are prominent throughout. One instance is the statement in the section on intravenous urography that "no renal surgery should ever be performed before a diagnosis has been confirmed by a retrograde pyelogram." Many urologists consider retrograde pyelography unnecessary, and even detrimental, in many cases of renal stone and in most cases of hydronephrosis. Doubtful cases will, of course, always require a check by the retrograde method. A valuable feature of the book is the concise history accompanying most of the illustrations. The publishers have cooperated splendidly with the author. The quality of the paper is excellent, and in each of the photographs the pathologic condition is clearly demonstrated.

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Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DERMATITIS IN WOOLEN MILL WORKERS

To the Editor:—**Certain employees in our local woolen mills develop a dermatitis of a pustular nature when handling the dyes and chemicals. The dyes used are all coal tar products; the chemicals are sodium bichromate, sodium sulfide, sulfuric acid, formic acid and acetic acid. Please discuss measures to protect workers from these materials, such as some type of ointment for the hands and arms.**

John J. Rouse, M.D., Reedsburg, Wis.

ANSWER.—Dermatitis among dyers in woolen mills is not uncommon. Most of it is due to sensitization to sodium bichromate, which is used as a mordant in the dye bath. The other chemicals mentioned (sodium sulfide, sulfuric acid, formic acid and acetic acid) are all primary skin irritants in strong concentration and sensitizers in low concentrations.

The best protective measures to be used by exposed workers are the wearing of impervious sleeves, gloves and aprons. These prevent contact of irritants with the skin. Protective ointments are less effective and in some cases not practical because they may come off on the wool. However, if protective ointments should be used, those of the water repellent type are the best. Such types can be obtained in either the greasy form or the dry film form. An ointment consisting of 70 parts of anhydrous lanolin and 30 parts of olive oil can be used for the greasy type of ointment. The water repelling dry type of ointment consists essentially of about 10 parts of shellac dissolved in isopropyl alcohol with a filler of talc, titanium oxide and sodium perborate. When applied to the skin, the alcohol evaporates and leaves a dry water repelling film of shellac in which is embedded the powders forming the white coating.

References:

Schwartz, Louis, and Tulipan, Louis: Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, pp. 218-219.

Schwartz, Louis, and Dunn, John E.: Dermatitis in a Woolen Mill, *Industrial Med.* **11**: 432 (Sept.) 1942.

EFFECTS OF REPEATED IRRADIATION

To the Editor.—**Dr. A states that the skin "throws off" x-ray effects after thirty days and that small doses of x-rays (used to treat eczematous conditions of the hands) may be repeated indefinitely, provided at least a month elapses between treatments. Dr. B states that (1) the skin can tolerate only a certain amount of x-rays over any one area during a person's entire life, that (2) no more should be given after this critical amount (1,200-1,600 roentgens) has been administered and that (3) the effect of radiation is cumulative and never lost; i. e., if a quantity of radiation was given at 20 years of age and then at 30 years of age, the total effect would be almost as harmful as if all were given within a short period. What is the present concept?**

M.D., Pennsylvania.

[This question was referred to two consultants whose respective replies follow.—EDITOR.]

ANSWER.—Dr. B is correct. The amount of roentgen radiation that is tolerated without grossly visible injury varies among individuals and depends on the size of the area exposed, the quality of the rays and the time over which the radiation is given. In general, permanent damage is done by more than 1,200 roentgens. Much smaller amounts may at times cause severe damage. Only a certain amount can be tolerated by any one area throughout a lifetime.

ANSWER.—Exactly how much x-rays the skin will tolerate is not known. The average American dermatologist administers 75 roentgens of low voltage unfiltered x-rays a week for a total of four to six weeks for the treatment of eczema of the back of the hands. This course of treatment is not repeated for at least a month. If it becomes necessary to administer further radiation the conservative dermatologist would not give to any one area of skin more than four courses of treatment (1,200 to 1,800 roentgens). More than this amount might lead to permanent radiation changes in the skin.

If a quantity of x-rays is administered which is just short of that required to produce radiodermatitis and ten years later a similar quantity is administered to the same area, radiodermatitis may ensue. The effects of x-rays are cumulative. It is unsafe to repeat small doses of x-rays indefinitely. (See MacKee, G. M., and Cipollaro, A. C.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 4, Philadelphia, Lea & Febiger, 1946.)

CAUSE OF INFANT DEATHS ON THE ZEBULON B. VANCE

To the Editor:—**In the Washington Letter in the June 15, 1946 issue of The Journal a paragraph entitled "Death of Babies Aboard Ship Traced to Virus Disease" appeared: "Representative Jackson, Democrat of Washington, reports that the War Department has revealed the cause of the deaths of eight servicemen's babies brought to the United States on the 'brideship' *Zebulon B. Vance* as a virus disease, pneumoenteritis. The disease has never occurred in human beings in this country before, it is reported. An army board of inquiry has absolved the medical staff of the ship of any negligence or misconduct regarding the deaths of the babies after arrival of the ship May 19 in New York from Le Havre." This spring an unusually severe type of infant diarrhea occurred in this locality. The usual methods of treatment seemed ineffective, and the best we could do was to give them supportive treatment and hope that they would weather the storm. Stool cultures were negative for the usual group of diarrhea organisms, and the possibility was considered that this might be the same disease as that on the "brideship." How was the conclusion reached that the epidemic diarrhea occurring on the ship was a new clinical entity? If it is a new clinical entity, how does it differ from the other diarrheal epidemics of suspected virus etiology in infants previously reported in this country? What were the autopsy findings?**

Fred C. Gregg, M.D., Tucson, Ariz.

ANSWER.—Apparently the press report of pneumoenteritis in infants on the *Zebulon B. Vance* was not founded on fact. On inquiry, a statement from the Surgeon General's Office is as follows: "It is our opinion at this time that this disease [on the *Zebulon B. Vance*] is not a new clinical entity, as further studies have failed to support such a conclusion."

INDICATIONS FOR CONTACT LENSES

To the Editor:—**A middle aged mother of two children, who has worn glasses since she was 14, is near sighted and somewhat astigmatic. She wants contact lenses. What are the advantages and disadvantages of contact lenses?**

M.D., New York.

ANSWER.—Advantages: Patients with keratoconus often can obtain but little improvement with common glasses. Keratoconus, as its name implies, is a change (occurring most frequently during puberty) in which the cornea protrudes in its center, taking the shape of a cone. The radius of curvature of the cornea in keratoconus is usually around 6 mm. and often is combined with irregular astigmatism and sometimes with superficial central opacities. Since the contact lens can correct these defects with a simple curved lens, the visual improvement is usually considerable.

Myopic patients who have a spectacle correction above 6 to 8 diopters cannot see much more than 20/30, owing to the fact that ordinary lenses, as they are some distance from the eye, reduce the size of objects seen through them. Many patients who have myopia even higher than that have a corneal curve of approximately 7.5 mm. The contact lens does not diminish the size of the object seen through it, and, as patients with 7.5 corneal curvature can have a contact lens with a base curve of 8.5, the visual improvement is such that they frequently attain 20/20 vision.

Patients with irregular or high astigmatism enjoy improved vision, since the corneal irregularity is replaced by a regular spherical curve. Patients with one aphakic eye often do not have binocular vision even when the vision is 20/20 in both eyes, owing to two factors: (1) The size of the image of the aphakic eye is approximately 25 per cent larger than the normal eye; (2) if the patient moves the eye behind ordinary lenses there is a prismatic effect that increases with the power of the plus lens. If the difference in size is corrected with iseikonic lenses the prismatic effect with the movement of the eyes will still be present and will make it impossible to attain fusion on lateral and especially vertical movement of the eyes.

Contact lenses diminish considerably the difference in the size of images received by the two retinas in aphakia and offer the best chance for fusion.

Another advantage of contact lenses is to be found in cases of corneal opacities which are not too dense to prevent fair visual acuity. These opacities are usually superficial and, besides the irregular astigmatism produced, they disturb optical imagery especially because they are located just at the line of separation of the different indexes of refraction; i. e., cornea 1.336 and air 1.00. This causes a more troublesome diffusion of light than if the opacity was located deeper in the cornea.

The contact lens, by covering the corneal opacity, places it relatively deeper to the anterior refractive surface. For practical purposes the index of refraction of the cornea is the same as the solution. Therefore the opacities, instead of being in line of separation of the two indexes of refraction, become located deeper and as a result the blurring is lessened.

Disadvantages: Many patients who wear ordinary lenses of the usual type think they can be replaced by contact lenses. Contact lenses do not give better vision than common glasses

when the refractive error is of low degree. Therefore, the patient will not see more with the contact lens than he would with his ordinary glasses. A contact lens is a foreign body which should be well placed and well fitted to the eye. It is not usually irritating if the fit and solution are correct and is not harmful to the eye; but often the patient feels as though he had something between the lids. This introduces a new sensation, to which the individual must become accustomed.

The "liquid lens," i. e. the solution placed between the lens and the cornea, infiltrates the corneal epithelium in the same way as water infiltrates the skin of the fingers when submerged a long time. This causes blurring of vision. The several solutions devised for this use have not as yet been perfected. The blurring of vision usually appears three to four hours after the contact lens has been in place, and when the lenses are removed from the eye the vision continues to be blurred for some time (usually fifteen minutes to half an hour). The employment of a contact lens requires a great deal of patience in coping with its adjustment, and those who can be benefited by these lenses are not always the ones psychologically suited for their use. A good rule to follow is: The more the patient needs the contact lens the better he is able to put up with its disadvantages.

TREATMENT OF NEUROSYPHILIS

To the Editor:—A woman aged 50 has a 4 plus blood Kline reaction and a 4 plus spinal fluid Kline reaction with a positive colloidal gold test. She does not give a history of primary or secondary lesions. Her general complaints are weakness and nervousness, and physical examination is entirely negative. Should the Army 30-60-03 treatment be given or should the more recent treatment be employed which is being used universally by veterans' hospitals at this time for all types of syphilis? This treatment consists of a total dosage of 2,800,000 units of penicillin in individual doses of 25,000 units intramuscularly every three hours around the clock for fourteen days; dichlorophenarsine is given concurrently on the first, fourth, seventh, tenth and thirteenth days of treatment intravenously in dosages of 1 mg. per kilogram of body weight to a maximum of 68 mg.; bismuth subsalicylate in oil in individual dosages of 200 mg. each given on the first, seventh and thirteenth days of treatment. Is the latter treatment justified, with the usual three month, six month, and one year follow-up?

M.D., Missouri.

ANSWER.—Before any treatment of this patient is undertaken she should (*a*) be examined by a competent neuropsychiatrist or by a syphilologist expert in the neuropsychiatric field and (*b*) she should have performed an adequate test of her spinal fluid, which includes a cell count performed on a freshly drawn specimen, quantitative estimation of protein content and complement fixation (Wassermann) test rather than any flocculation test, and the details of the colloidal gold or other colloidal test should be known.

From the inquirer's statement the only diagnostic comment which can be made is that the patient has neurosyphilis. This, is not, however, the important consideration in treatment. Instead, it is essential that the attempt be made accurately to delineate the type of neurosyphilis which the patient has.

In any case neither of the treatment systems suggested by the inquirer is suitable. Almost certainly it is desirable for the patient to be treated with fever by means of induced tertian malaria, combined with the simultaneous administration of somewhere between 4 and 10 million units of penicillin.

After treatment is given with fever plus penicillin, follow-up should extend over a period of many years rather than a single year or less.

TREATMENT OF THROMBOANGIITIS OBLITERANS

To the Editor.—A man with severe thromboangiitis obliterans has been relieved somewhat by Depropanex but has not improved very much. Are there any new drugs that might be of value?

L. O. Simenstad, M.D., Osceola, Wis.

ANSWER.—Unfortunately, medication is not available at present which is highly effective in the relief of thromboangiitis obliterans. Depropanex, the product mentioned in the query, is a proprietary preparation consisting of a deproteinated pancreatic extract. It is a saline solution of a protein free, nitrogenous fraction obtained by acid-alcohol treatment of beef pancreas free from insulin, histamine and acetylcholine. This proprietary preparation is recommended by the manufacturers as a vasodilator and antispasmodic. The reports on its use vary greatly, some favorable, others that it is of little or no value. Animal experiments with this product indicate that it is not absorbed following oral administration. Injections of typhoid H antigen have been used for years as a vasodilator in cases of thromboangiitis obliterans with some benefit, but it has not proved uniformly successful, and there are certain disadvantages. Increase of fluid intake with sodium chloride has been used to produce hydremia, with occasional beneficial results. Xanthine derivatives or papaverine hydrochloride may be tried to relax spastic vessels or dilate collateral channels.

A new drug which will be on the market soon, and which is already reported in the literature, namely, tetraethyl ammonium bromide, has given as promising results as any medical therapeutic measure yet developed. In some cases injection of this chemical for three or four days has given relief over a period of several weeks.

The surgical treatment of thromboangiitis obliterans must be seriously considered. It is of special value before ulceration has occurred. The efficiency of the collateral circulation may be greatly increased, and in some cases the extremity, even when extensive ulceration is present, may be saved by lumbar sympathectomy.

TRAUMA OF TONGUE AND POSSIBLE RHABDOMYOMA

To the Editor:—A man aged 30 bit the anterior third of the dorsum of the tongue while eating. Examination ten days later revealed a painless nodular, circumscribed mass 3 mm. in diameter covered with normal epithelium. Submaxillary adenopathy was not present. The mass was removed. Pathologic study showed traumatized striated muscle fibers in the deeper parts of the section which had undergone a certain amount of discoloration. The continuation of these fibers toward the periphery showed pathologic changes; their nuclei had become large and vacuolated and each contained a large prominent nucleolus. Syncytial formations containing such nuclei were seen. Toward the mucosa especially around the vessels these cells were spindle shaped, and mitotic figures were seen.

The possibilities have been considered that, as a result of the trauma, the striated muscle has undergone a malignant rhabdomyomatous transformation or that this change may be a simple reaction to the trauma and will heal in time. Is this a malignant manifestation or a normal muscle tissue reaction to the trauma? If it is suggestive, what treatment is advisable?

A. Hovnanian, M.D., Aleppo, Syria.

ANSWER.—There is no evidence in the pathologic report of any rhabdomyomatous transformation. The appearances described are those of healing of injury to muscle and regeneration.

22,000,000 VOLT ELECTRON TREATMENT OF CANCER

To the Editor:—A patient with inoperable cancer has asked information about 22,000,000 volt electron treatment of carcinoma printed in a United Press story from Chicago July 18, 1946. Please discuss this treatment.

Hamlin Mattson, M.D., Minneapolis.

ANSWER.—As far as is known, cancer patients have not been treated with 22,000,000 volt electrons, nor have 22,000,000 volts of x-rays been used in the treatment of cancer.

TISSUE THERAPY OF RETINITIS PIGMENTOSA

To the Editor:—My attention has been called to the inquiry, on page 117 of the issue of Sept. 14, 1946 under Queries and Notes on the tissue therapy of retinitis pigmentosa. The statement is made that "as far as is known there are no ophthalmologists in this country using Filatov's technic or conducting investigations on his work." I have been intensively studying Filatov's work in relation to retinitis pigmentosa at the New York Hospital since June of this year. So far the method has been used on over 40 patients. It is entirely too early to offer any report on this work except that we have had some encouraging results and are going to continue the investigation along various lines to determine its merits and to work out plans of treatment. I must emphasize the fact that the work is experimental and by no means in the "cure" stage. Those samples of Filatov's work on "tissue therapy" which have appeared in this country have been sketchy and are not entirely up to American scientific standards in completeness or length of follow-ups. The methods are not as simple as they sound, and we have run into some bad reactions. Some of these in private practice could lead to legal difficulties. The method merits further study both because of Filatov's good reputation and because of the few encouraging results which we have seen. However, because of the very nature of this work it should be done only in a few large centers which have ample material and facilities to give it a fairly comprehensive test. I believe that it will be found that this will lead to considerable modification of the method of usage and of the materials employed. Even Filatov does not believe that his method is the last word in the therapy of retinitis pigmentosa. It is still far from being an established therapeutic procedure and is not yet adaptable for ordinary office routine. Retinitis pigmentosa is not a common disease. It would certainly be unfair, and perhaps dangerous, for many individuals to attempt this investigative work on a mere handful of patients and then to draw conclusions.

Dan M. Gordon, M.D., New York.

To the Editor:—Aided by a grant from the Council on Pharmacy and Chemistry of the American Medical Association and by another grant from the American-Soviet Medical Society, we are investigating and using Filatov's technic in the treatment of retinitis pigmentosa. Our experiments are being done under controlled conditions and with special attention to dark adaptation studies of the retina. The work is being carried out in the departments of ophthalmology and physiology of the New York Medical College, Flower and Fifth Avenue Hospitals.

Samuel L. Saltzman, M.D.
Charles Haig, Ph.D.
New York.

Assistant Clinical Professor of Ophthalmology and Assistant Professor of Physiology, Respectively.

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